Docket Number: EPA-HQ-OPP-2009-0308
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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Agency Response to the Natural Resources Defense Council's (NRDC) April 2009 Tetrachlorovinphos Petition

July 21, 2020

for

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List of Acronyms and Abbreviations

AChE	Acetylcholinesterase
A.I.	Active Ingredient
ALJ	Administrative Law Judge
APA	Administrative Procedure Act
BEAD	Biological and Economic Analysis Division
DAF	Dermal Absorption Factor
DCI	Data Call-In
EPA	Environmental Protection Agency
ET	Exposure Time
F_{AR}	Fraction Application Rate
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
HEC	Human Equivalent Concentration
LOC	Level of Concern
MOA	Mode of Action
MOE	Margin of Exposure
NOIC	Notice of Intent to Cancel
NRDC	Natural Resources Defense Council
OP	Organophosphate
ORE	Occupational and Residential Exposure
POD	Point of Departure
RBC	Red Blood Cell
RfC	Reference Concentration
RED	Reregistration Eligibility Decision
SAP	FIFRA Scientific Advisory Panel
SOP	Standard Operating Procedure
TC	Transfer Coefficients
TCVP	Tetrachlorvinphos
TR	Transferable Residue Measure
TRED	Tolerance Reassessment Eligibility Decision
UE	Unit Exposure
UF_{DB}	Database Uncertainty Factor
USDA	United States Department of Agriculture

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I. Executive Summary

This document constitutes the Environmental Protection Agency's (EPA or the Agency) response to the Natural Resources Defense Council's (NRDC) Petition dated April 23, 2009 (Petition) requesting that EPA cancel all pet uses of the pesticide tetrachlorvinphos (TCVP). The factual background relevant to NRDC's Petition is discussed in Section II of this document. Section III explains EPA's new conclusions related to any potential risks associated with the pet uses. Section IV discusses the benefits TCVP pet products provide their users and the potential impacts associated with the changes necessary to address risks of concern. Section V provides specifics on how EPA has addressed any identified risks of concern. For the reasons discussed below, EPA is denying NRDC's Petition to cancel all pet uses for TCVP.

As discussed in Section III, in response to NRDC's Petition, EPA conducted a revised residential exposure and risk assessment in 2020 for all TCVP pet product uses. TCVP pet uses consist of liquid sprays, dusts, and collars. Based on the revised residential exposure and risk assessment for TCVP, EPA does not find risks of concern resulting from liquid spray pet uses of TCVP and therefore declines today to initiate cancellation action against such uses as requested in the Petition. The registrants for the remaining registrations for products containing TCVP with uses on cats and dogs have agreed to either voluntarily cancel those products or amend those products such that revised risk estimates result in no risks of concern. Specifically, the registrants, The Hartz Mountain Corporation (Hartz) and Chem-Tech Ltd. (Chem-Tech), have submitted requests under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) section 6(f) [1] to either terminate uses on cats and dogs from their dust products or request voluntary cancellation of their dust products and EPA is processing those requests; Hartz has submitted a request under FIFRA section 6(f) to voluntarily cancel EPA Registration No. 2596-63, a cat collar; and Hartz has requested label and registration amendments for certain other pet collars, which EPA is currently evaluating. With these changes, EPA does not find risks of concern. (*See "Tetrachlorvinphos: Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses"* and *"Tetrachlorvinphos: Addendum to the Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses" in Attachments B and C*).

In addition to the registrants, there are supplemental distributors associated with these registrations. Under 40 CFR 152.132, a registrant may distribute or sell their product under another person's name and address instead of their own. The distributor is an agent of the registrant, and both the registrant and the distributor may be held liable for violations pertaining to the distributor product. When the registered product is cancelled or amended, so too is the distributor product. Therefore, all changes made by the registrants must also be made by the supplemental distributors. A full list of the associated supplemental distributors can be found in Attachment A.

While EPA's revised 2020 residential exposure and risk assessment for TCVP addresses the arguments raised in NRDC's Petition regarding whether TCVP pet uses pose unacceptable risks, the 2020 assessment and the registration review currently underway address the issues

[1] In this document EPA uses the U.S. Code citations as well as the more commonly known FIFRA sections.

noted by NRDC as they relate to the 2006 TCVP Reregistration Eligibility Decision (RED). To the extent that NRDC suggests that EPA perform a new organophosphate (OP) cumulative risk assessment, EPA is currently reviewing the organophosphates as a whole (including TCVP) in registration review pursuant to FIFRA section 3(g), and 40 CFR Part 155, which includes a new OP cumulative risk assessment.

II. Background

TCVP is a member of the organophosphate (OP) class of pesticides. Like other OPs, TCVP's mode of action involves the inhibition of the enzyme acetylcholinesterase (AChE). TCVP was first registered as a pesticide in 1966 and is an insecticide used to control fleas, ticks, various flies, lice, and insect larvae on livestock and domestic animals and their premises. TCVP is also applied as a perimeter treatment. All crop uses of TCVP were voluntarily cancelled in 1987.

The RED for TCVP was initially completed in September 1995. An interim Tolerance Reassessment Eligibility Decision (TRED)[2] for TCVP was completed in July 2002. A residential exposure assessment was originally completed in 1999[3] in support of the TRED, which concluded that there were no residential risks of concern resulting from handler and post-application exposure. The residential assessment was refined in 2002. Both the TRED and 1999 assessment can be found at www.regulations.gov in public docket numbers EPA-HQ-OPP-2002-0295 and EPA-HQ-OPP-2008-0316. The Agency completed the OP cumulative risk assessment (considering all OPs, including TCVP, sometimes referred to as the "OP Cumulative") in December 2001, and, as a result, the TCVP TRED and RED were considered final at that time and can be found in public docket number EPA-HQ-OPP-2006-0618. Updates to the OP Cumulative risk assessment were completed in June 2002 and July 2006[4]. There were no risks of concern identified in the residential assessment portion of the OP Cumulative, which considered exposure from the pet uses of TCVP along with all other OP uses.

A. Registration Review of TCVP

Following reregistration and tolerance reassessment, EPA is required to complete the next re-evaluation of TCVP under the FIFRA section 3(g) registration review program by October 1, 2022. The registration review program is intended to make sure that, as the ability to assess and reduce risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically re-evaluates pesticides to make sure that as these changes occur, products in the marketplace can continue to be used without causing unreasonable adverse

[2] Available at https://www.regulations.gov/document?D=EPA-HQ-OPP-2002-0295-0012.
[3] Available at https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0316-0010.
[4] Available at https://www.regulations.gov/document?D=EPA-HQ-OPP-2006-0618-0002.

effects on human health and the environment taking into account the risks and benefits associated with the use of the product.[5]

The TCVP registration review docket opened in June 2008 with the TCVP Summary Document and supporting documents[6] stating what EPA knew about TCVP at that time and what additional risk analyses and data were needed to make a registration review decision. A Generic Data Call-In (GDCI) was issued December 29, 2009, requiring the submission of studies to inform the Agency's evaluation of risk from all TCVP exposure pathways, including those related to pet uses. The TCVP Task Force, comprised of the TCVP registrants, committed to conducting the studies, and anticipated submission beginning March 2012.

Concurrent with the TCVP Task Force's data development for registration review, the Agency expedited its review of the risk from pet uses to address NRDC's petition. The Agency began with a summary of pet collar risk estimates from the RED in order to frame the path forward for updating the pet use risk assessment in the February 2010 memorandum, *Tetrachlorovinphos, PC Code 083701, DP Barcode 346880: Summary of Pet Collar Risk Estimates*. This memorandum outlined the risk assessment methods that changed since the previous assessment for the TCVP RED and identified significant uncertainties that needed to be addressed in a new risk assessment. EPA completed an updated TCVP assessment on the pet uses on November 5, 2014, *Residential Exposure Assessment in Response to the Natural Resources Defense Council Petition to Cancel All Pet Uses for Tetrachlorvinphos* ("2014 Pet Products Assessment"), in advance of the Agency's comprehensive December 21, 2015 TCVP Draft Human Health Risk Assessment for registration review, in continued efforts to expedite a response to NRDC's Petition.

In January 2016, EPA took the study *Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos*, Journal of Exposure Science and Environmental Epidemiology, Davis, M. et al., v.18, 564-570 (2008)) ("Davis Study") to the Human Studies Review Board (HSRB) to determine if the Agency could rely on the study. 40 CFR 26.1703 prohibits EPA from relying on data from any research involving intentional exposure of any pregnant human subject (and therefore her fetus), nursing woman, or child, unless the EPA has: (a) obtained the views of the HSRB; (b) provided an opportunity for public comment on the proposal to rely on the otherwise unacceptable data; (c) determined that relying on the data is crucial to a decision that would impose a more stringent regulatory restriction to protect public health than could be justified without the data; and (d) published a full explanation of the decision to rely on the data, including a thorough discussion of the ethical deficiencies of the underlying research and the full rationale for finding that the standard in item (c) was met.

The HSRB concluded that: "The research is scientifically sound and, if used appropriately, the pet fur transferable residue data from the rubbing protocol used in the study

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[5] *See* FIFRA section 2(bb).

[6] Available at https://www.regulations.gov/docket?D=EPA-HQ-OPP-2008-0316.

can provide useful information for evaluating potential exposures of adults and children from contact with dogs treated with tetrachlorvinphos containing pet collars."[7]

EPA subsequently completed the TCVP Revised Human Health Risk Assessment for Registration Review, dated December 21, 2016, in which post-application risks were assessed using the Davis Study data. The December 21, 2016 risk assessment also assessed pet collars using assumptions of varying ratios of liquid/dust of active ingredient in the exposure calculations to determine the impact on the outcome of the assessment. At the time, EPA was uncertain as to whether the active ingredient in the collars should be considered a liquid or a solid, or some percentage of both liquid and solid, for purposes of risk assessment. This risk assessment was posted in the docket[8] on December 29, 2016.

EPA issued a Data Call-In (DCI)[9] to Hartz on June 3, 2019 requiring a mechanical torsion study in order to resolve the remaining uncertainty regarding the collar formulation. Hartz submitted the study on August 28, 2019. EPA has since reviewed this data and determined it is acceptable for inclusion in its revised residential exposure and risk assessment discussed in Section III.

EPA has incorporated the mechanical torsion data in its July 2020 revised residential exposure and risk assessment "*Tetrachlorvinphos: Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses.*"[10] The registrants have agreed to mitigate risks identified in the revised residential pet product assessment, so EPA also completed an addendum, *Tetrachlorvinphos: Addendum to the Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses,"* which reflects the amendments to those registrations and confirms that the revised risk estimates result in no risks of concern. The revised residential exposure and risk assessment and addendum are available in Attachments B and C, respectively.

While EPA has completed the revised residential exposure assessment in order to expedite its response to the NRDC Petition, TCVP remains under registration review pending completion of a full revised human health risk assessment (including an aggregate assessment together with all TCVP uses) and registration review decision. Completion of the draft full registration review human health risk assessment is anticipated in 2021, followed by a 60-day public comment period. EPA will subsequently issue a Proposed Interim Decision that responds to any public comments received on the draft registration review revised human health risk assessment, and which will also be available for a 60-day public comment period. EPA will issue an Interim Decision by October 2022.

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[7] See https://www.epa.gov/sites/production/files/2016-04/documents/hsrb_final_report_january_2016_meeting_-_3-30-2016.pdf

[8] Available at https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0316-0055.

[9] Available at https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0316-0078.

[10] Available at https://www.regulations.gov/docket?D=EPA-HQ-OPP-2008-0316.

B. Summary of NRDC's Petition to Cancel All Pet Uses

On April 24, 2009, EPA received a Petition under the Administrative Procedure Act (APA), 5 U.S.C. § 551, et seq., from NRDC, dated April 23, 2009, to cancel all pet uses of TCVP, as well as an April 2009 "Issue Paper" issued by NRDC entitled "Poisons on Pets II: Toxic Chemicals in Flea and Tick Collars." The Petition raised the following issues:

- NRDC argued that EPA failed to consider pet collar exposures in the 2002 revised human health risk assessment underlying the 2006 RED. NRDC argued that despite finding that pet collar uses provided the highest exposure levels for adults, EPA still chose not to conduct a risk assessment for pet collars, and that EPA ignored the possibility that the pet collar uses could expose infants and children to unsafe levels of TCVP.
- NRDC argued that EPA used faulty exposure assumptions in the 2006 organophosphate cumulative risk assessment. NRDC argued that the EPA's organophosphate cumulative risk assessment for pet products significantly underestimated toddlers' exposure to pesticide residue on a pet from TCVP pet products, particularly flea collars.
- NRDC argued that use of TCVP pet collars results in unacceptably high exposures, pointing to NRDC's April 2009 "Issue Paper" entitled "Poisons on Pets II: Toxic Chemicals in Flea and Tick Collars," and to a 2008 study entitled "*Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphate Insecticide Tetrachlorvinphos*," Journal of Exposure Science and Environmental Epidemiology, Davis, M. et al., v.18, 564-570 (2008) (the "Davis Study").

The Petition concluded that EPA's 2006 RED for TCVP is "arbitrary and capricious, and contrary to law," and that "EPA must … cancel all pet uses of [TCVP]." Petition at 6.

On June 5, 2009, EPA announced receipt of NRDC's Petition and "Issue Paper" in the Federal Register (74 FR 27035) and posted the Petition in public docket number EPA-HQ-OPP-2009-0308 in regulations.gov for a 60-day public comment period, during which time interested stakeholders could review and comment on the Petition.

During the comment period, EPA received approximately 8,600 form letters as part of a mass campaign supporting NRDC's Petition. The Agency also received a comment from The Humane Society of the United States (HSUS) that supported NRDC's Petition, and a comment from Hartz, which opposed NRDC's Petition. In addition, Hartz provided additional information, including a dislodgeable residue study, to help refine the Agency's pet use risk assessment. EPA considered the substantive comments received during that public comment period in 2009 and released a Response to Comments document[11] concurrently with the Agency's initial response to the NRDC Petition in 2014, as discussed in further detail in section II.D. of this document below. Consistent with EPA's Response to Comments document, the Agency has continued to review new information and this response to NRDC's Petition includes updated risk and benefit assessments.

[11] Available at https://www.regulations.gov/document?D=EPA-HQ-OPP-2009-0308-0012.

C. EPA's Review of NRDC's Issue Paper

As mentioned above, along with the Petition, NRDC submitted an April 2009 NRDC "Issue Paper" entitled "Poisons on Pets II: Toxic Chemicals in Flea and Tick Collars" (hereinafter "Poison on Pets II") for EPA's consideration of potential exposures from TCVP pet collars. This "Issue Paper" consisted of a study overview and summarized findings along with a methodological appendix but did not include the full study report including all the raw data. In a letter dated May 28, 2009, the Agency requested additional scientific information from NRDC so that EPA could fully analyze and independently verify the results of the study report, including all raw data and the protocol for the pet residue study. EPA also requested information on the ethical conduct of the study regarding the use of human subjects, as required by 40 CFR § 26.1303 under Subpart M – "Requirements for Submission of Information on the Ethical Conduct of Completed Human Research."

On June 25, 2009, NRDC submitted a response letter.[12] Although NRDC's June 25, 2009 letter included a copy of the original protocol intended to support NRDC's argument that the studies underlying the "Poison on Pets II" report were not "human studies" under 40 CFR Part 26, the letter did not include either the scientific information to enable EPA to verify the results of the study report or the information on the ethical conduct of the studies required by 40 CFR § 26.1303. NRDC's letter stated:

> "… NRDC will await EPA's final determination that the study does not constitute research with human subjects and that the Agency will include it as part of its assessment of our Petitions. Once EPA makes that final determination, then we will provide the underlying data supporting our report." NRDC Letter, June 25, 2009, at 3.

In a letter dated August 7, 2009, EPA informed NRDC that the Agency (EPA's Office of Pesticide Programs, in consultation with EPA's Human Subjects Research Review Officer in the Office of the Science Advisor) still regarded the two studies described in the "Poison on Pets II' report as research with human subjects covered by EPA's rules in 40 CFR Part 26, "Protection of Human Subjects."[13]

To date, NRDC has not submitted the necessary raw data to allow EPA to verify the "Poisons on Pets II" study report findings. Without the raw scientific data, this information was not considered in EPA's evaluation of NRDC's Petition.

D. EPA's Initial Response to NRDC's Petition and Subsequent Litigation

On April 23, 2009, NRDC filed a Petition under the APA asking EPA to cancel all pesticide registrations for the use of TCVP to control fleas and ticks on pets ("pet uses").

As of February 2014, EPA had not responded to NRDC's 2009 Petition and NRDC filed a mandamus Petition in the U.S. Court of Appeals for the D.C. Circuit to compel a response. In

[12] Available at https://www.regulations.gov/document?D=EPA-HQ-OPP-2009-0308-0006.
[13] Available at https://www.regulations.gov/document?D=EPA-HQ-OPP-2009-0308-0007.

November 2014, EPA completed a new risk assessment in response to NRDC's 2009 Petition and, on the basis of that risk assessment, denied NRDC's Petition. NRDC's 2014 mandamus Petition was therefore dismissed as moot in December 2014.

In January 2015, NRDC filed suit in the U.S. Court of Appeals for the Ninth Circuit on the merits of EPA's denial of its APA Petition. In its August 5, 2015 Opening Brief, NRDC raised for the first time the issue of whether the TCVP in pet collars should be considered a liquid or solid formulation. While EPA had previously categorized the active ingredient in all pet collar products as liquid formulations as supported by the best available science at the time of development of the relevant Standard Operating Procedure (SOP),[14] NRDC's August 5, 2015 Opening Brief pointed out that the label for Hartz UltraGuard Flea and Tick Collar for Dogs (EPA Reg. No. 2596-84) at the time stated that "as the collar begins to work, a fine white powder will appear on the surface."

In 2015, while the Ninth Circuit litigation was on-going, and as scientific methodologies and understanding had evolved, EPA reconsidered its position for purposes of developing the TCVP Revised Human Health Risk Assessment for Registration Review (which would ultimately be issued December 21, 2016, and posted to the docket on December 29, 2016)[15] by (re)assessing pet collars containing TCVP using assumptions of varying ratios of liquid/dust (1/99, 50/50, and 99/1) in the collar. These varied assumptions were incorporated into the exposure calculation to account for the uncertainty in the liquid/dust ratio. Without having chemical-specific composition information related to TCVP pet collars, this approach was taken to account for the range of possibilities which could occur. EPA also determined that an additional 10X uncertainty factor should be applied to TCVP to address uncertainties in the dose-response relationship for neurodevelopmental effects for the OPs in infants, children, and women of childbearing age for all residential exposure scenarios. In September 2015, EPA therefore sought a voluntary remand of its 2014 denial of NRDC's 2009 APA Petition. In arguing for remand without vacatur, EPA informed the Court and parties that it intended to issue a new risk assessment before the end of 2016 and respond to the Petition within 90 days after the final risk assessment was issued. In June 2016, the court granted EPA's motion for remand and denied NRDC's motion for vacatur.

In addition, as mentioned above, in January 2016 EPA took the Davis Study to the HSRB, which concluded that the study was scientifically valid and met the appropriate human ethics requirements. EPA therefore relied on the Davis Study in developing the December 21, 2016 TCVP Revised Human Health Risk Assessment for Registration Review, as the Davis study provided transferable residue data for pet fur and resulted in greater potential risks than those estimated using the pet collar residue transfer study EPA had relied upon in previous assessments.

As also mentioned above, EPA completed a new TCVP Human Health Risk Assessment on December 21, 2016 (posted to the docket on December 29, 2016).[16] While that risk

[14] Available at https://www.epa.gov/sites/production/files/2015-08/documents/usepa-opp-hed_residential_sops_oct2012.pdf.
[15] Available in regulations.gov at https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0316-0055.
[16] Available in regulations.gov at https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0316-0055.

assessment identified some potential risks of concern, the risk assessment left unresolved some key questions, such as whether the TCVP in the pet collars should be considered "liquid" or "solid" (which, in turn, could affect the assessment of risk). With the remaining uncertainty around the physical form of TCVP present in the collars, the Agency was unable to fully respond to NRDC's Petition. Therefore, on March 21, 2017 (90 days after finalizing the new TCVP risk assessment), EPA informed NRDC that EPA intended to merge the Petition response with its TCVP registration review decision under FIFRA section 3(g) that was then-scheduled to be issued in the fall of 2017.

EPA's assessment of the pet collars hinged on the uncertainty regarding the physical form of TCVP in collars, and the Agency determined that the best solution for identifying the physical form of TCVP released from each pet collar would be to require a composition study from the registrant of the pet collars, Hartz. Therefore, EPA issued a Data-Call-In (DCI) to Hartz on June 3, 2019, pursuant to FIFRA section 3(c)(2)(B), requiring a composition study in the form of a mechanical torsion study.[17] This study, along with additional transfer residue data, were submitted to the Agency on August 28, 2019. The Agency completed the review of these data in December 2019; the results of these studies are discussed further in Section III. The Agency has incorporated these data into the July 2020 revised residential exposure and risk assessment. The data evaluation records for these data are available in public docket EPA-HQ-OPP-2008-0316 at www.regualtions.gov.[18]

Five days before EPA issued the DCI, on May 29, 2019, NRDC filed a mandamus Petition with the Ninth Circuit Court of Appeals asking the Court to order EPA to respond to NRDC's 2009 Petition. On April 22, 2020, the Court issued an Order directing EPA to either initiate cancellation of the TCVP pet use registrations or deny NRDC's 2009 Petition within 90 days of the Court's order (i.e., by July 21, 2020). The Court further ordered that if EPA initiates cancellation, the Agency must file status reports with the court every 2 months and stated that the Court expects cancellation to conclude within 1 year of the Court's order absent a showing of good cause for any longer period.

III. EPA's Revised Residential Exposure and Risk Assessment

EPA conducted a revised residential exposure assessment for all TCVP pet uses. While EPA's updated 2020 pet-product risk assessment (and addendum to the risk assessment) addresses EPA's assessment of the pet uses, the registration review risk assessment currently underway addresses all uses of TCVP. Like reregistration, registration review considers all the uses of an active ingredient along with new data and other information to ensure that the pesticide continues to meet the standard for registration under FIFRA. To the extent that NRDC's 2009 Petition may be suggesting that EPA perform a new cumulative risk assessment, EPA is currently reviewing the organophosphates (OP) as a whole (including TCVP) in registration review pursuant to section 3(g) of FIFRA, which includes a new OP cumulative risk assessment. EPA has determined it is unnecessary to update the cumulative risk assessment to respond to NRDC's requests to cancel all TCVP pet uses.

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[17] Available in regulations.gov at https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0316-0078

[18] Available at https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0316-0083 and https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0316-0084.

In developing a response to this Petition, EPA considered, among other things, the information contained in the Petition, new data relevant to the assessment of exposure from pet collars (i.e., additional Hartz studies: MRID 50881801/ D453149 and MRID 50931601/ D454190), and updated residential exposure assessment methodologies and reevaluation of existing data (i.e., the Davis Study). The Agency completed a revised residential exposure and risk assessment for all TCVP pet product uses, entitled "*Tetrachlorvinphos: Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses*" (attached hereto as Attachment B). In addition, the Agency completed an addendum to that risk assessment (*Tetrachlorvinphos: Addendum to the Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses*) that incorporates mitigation measures proposed by the registrant to address risk concerns with several pet collars (attached hereto as Attachment C). The addendum (based on the 2020 revised residential exposure assessment) evaluates the risks associated with certain pet collars in the case that the requested mitigation measures are approved by EPA, and, if so, there will no longer be any risks of concern associated with TCVP pet products for all exposure scenarios. The key points of the 2020 revised residential exposure and risk assessment are outlined below, as part of the evaluation of NRDC's claims in its Petition.

EPA risk assessments rely on the most recent guidance and risk assessment methodologies available at the time they are completed. The human health risk assessments that NRDC's Petition alleges failed to properly identify risks were originally completed in 1999 and 2006 and utilized exposure assumptions and methodologies based on Standard Operating Procedures (SOPs) for pet product risk assessments in place at that time. Since 2012, TCVP residential pet product assessments assessed residential handler and post-application risk from exposure to TCVP pet products using the Agency's 2012 SOPs for Residential Pesticide Exposure Assessment.[19] Development of the 2012 SOPs included external peer review, including the Agency presenting a draft of the SOPs to the FIFRA Scientific Advisory Panel (SAP) for comment in 2009. The revised residential exposure assessment also incorporates the following changes since the previous assessment in 2016:

- updated application rates for certain pet collars,
- incorporation of additional pet collar specific TCVP transferable residue and formulation type (i.e., liquid/solid) data that were submitted since the last assessment[20], and
- inclusion of an adjustment factor for trimming of pet collars when applied to animals (i.e., 20% removal after application).

The following is a summary of the analysis and conclusions found in the July 2020 revised residential exposure assessment, entitled "*Tetrachlorvinphos: Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses.*"

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[19] https://www.epa.gov/sites/production/files/2015-08/documents/usepa-opp-hed_residential_sops_oct2012.pdf

[20] Transferable residue studies: MRIDs 50719201, 50719202, 50881801, and 50881802; torsion" composition study, MRID 50931601.

A. Toxicology and Uncertainty Factors

Like other OPs, the mode of action (MOA) for TCVP involves inhibition of the enzyme acetylcholinesterase (AChE) via phosphorylation of the serine residue at the active site of the enzyme. This inhibition leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system.

TCVP has low acute toxicity by the oral, dermal, and inhalation routes of exposure. It is a slight dermal irritant, a moderate eye irritant, and a dermal sensitizer. TCVP is classified as a possible human carcinogen (Group C) based on statistically significant increases in combined hepatocellular adenoma/carcinomas in mice, and suggestive evidence of thyroid c-cell adenomas and adrenal pheochromocytomas in rats. The mutagenicity database for TCVP suggests that this chemical was not mutagenic in either the gene mutation assay or the primary rat hepatocyte unscheduled DNA synthesis assay. This chemical was positive for inducing chromosomal aberrations in Chinese hamster ovary cells in the absence of metabolic activation, but was negative in the presence of metabolic activation. Immunotoxicity was not observed at dose levels that exceed the limit dose.

As with other OPs, TCVP exhibits a phenomenon known as steady state AChE inhibition. After repeated dosing at the same dose level, the degree of inhibition comes into equilibrium with the production of new, uninhibited enzyme. At this point, the amount of AChE inhibition at a given dose remains consistent across duration. In general, OPs reach steady state within 2-3 weeks; a pattern that is observed for most OPs, but not every OP, like TCVP, which shows no difference in response across duration. For TCVP, the steady state is reached after a single day of exposure. As such, the endpoint selection for TCVP considers data available for all durations of dosing when choosing the most protective point of departure.

No quantification of dermal non-cancer risk is required for TCVP since there were: (1) no treatment-related effects (no clinical signs) at doses up to and including the limit dose of 1000 mg/kg/day in the dermal toxicity study; (2) both red blood cell (RBC) and brain cholinesterase activity were assessed in the dermal study and neither compartment was affected at the limit dose; and (3) no quantitative susceptibility was observed for juvenile or gestational lifestages in the developmental, reproductive, or comparative cholinesterase assay (CCA) toxicity studies. Despite the determination of the lack of non-cancer dermal hazard for TCVP, dermal exposures from TCVP must be quantified for the purpose of cancer risk assessment. Because the cancer assessment is based on an oral study, a dermal absorption factor (DAF) of 9.6% was used in the route-to-route extrapolation. The DAF is based on the results of a dermal penetration study in rats.

For TCVP, EPA has determined that a database uncertainty factor (UF_{DB}) of 10X is necessary to be added to address uncertainties in the dose-response relationship for neurodevelopmental effects for the OPs in infants, children, and women of childbearing age for all residential exposure scenarios.

For the residential incidental oral exposures, the level of concern (LOC) is 1000 (i.e., risk estimates are not of concern when the margin of exposure (MOE) is $\geq$ the LOC) which includes

a 10X uncertainty factor for interspecies extrapolation, a 10X uncertainty factor for intraspecies variation, and a 10X additional UF_{DB}. For the residential inhalation exposures, the LOC is 300 which includes a 3X uncertainty factor for interspecies extrapolation, a 10X uncertainty factor for intraspecies variation, and a 10X additional UF_{DB}. The interspecies extrapolation factor for the inhalation route has been reduced from 10X to 3X because the reference concentration (RfC) methodology for inhalation has been used to determine a human equivalent concentration (HEC) and takes into consideration the pharmacokinetic differences between animals and humans.

B. Residential Handler Exposures

In the revised residential exposure assessment, EPA identified that there is the potential for residential exposures from the use of TCVP pet products. Residential handler exposures to TCVP pet products may occur via the dermal or inhalation routes while the product is placed on a cat or dog. A steady-state non-cancer residential handler exposure assessment (inhalation only; no dermal point of departure (POD) selected) was performed for homeowners applying TCVP products to cats and dogs. In addition, a residential handler cancer assessment was conducted due to TCVP being classified as a Group C possible human carcinogen with a linear low-dose approach for quantification of risk using the oral slope factor (Q1*) of 1.83×10^{-3} $(mg/kg/day)^{-1}$.

1. Residential Handler Assumptions and Inputs

Application Rates for all Pet Uses: The following provides a summary of the application rates per type of TCVP pet use. For TCVP dust and powder products, all products identify a specific amount to use per animal weight that allows for determination of the maximum application rate. For example, label directions will state to use a certain amount of product (e.g., ounces of product) per size of pet (small versus large animal) which allows for calculation of the total pounds of active ingredient to be applied when the percent active ingredient in the product is known.

For TCVP liquid sprays (trigger and pump spray products), all registered products direct the user to apply a specific number of "strokes" per animal size. In order to determine the amount of active ingredient (a.i.) applied per treatment as specified by number of strokes, EPA requested additional information and received data from a product registrant. The registrant provided information regarding the total volume of product released per stroke for pump and trigger spray products: 0.19 and 0.93 grams, respectively. Only trigger spray products are available for dogs; however, both pump and trigger spray products are available for cats. Additionally, in 2014, EPA approved an amendment for the registrant's product label of EPA Reg. No. 2596-140 that now includes a recommended number of strokes per animal size. The specific number of strokes per animal size is located in Table 4.0 in the 2014 residential assessment and Table A.2 of the 2020 revised residential exposure assessment. Previously, the label did not specify a number of strokes per cat/dog. The recommendation of strokes provided a range for the assessment, assuming that the user follows the label.

For pet collars, the application rates used in risk assessments typically represent the maximum amount of a.i. that could be applied by weight of the treated animal (small, medium,

and large). This is only possible when the product is manufactured for use, or is labeled specifically, for different animal weight ranges. If EPA does not have this information, a number of assumptions are used (as described in HED's 2012 Residential SOPs (Treated Pets SOP)). The majority of pet collar formulations are registered as a single collar for use on all animal weight ranges. These have been assumed for use on different weight ranges as specified in the Residential SOPs which include:

- Cats – Small (up to 5 lbs), Medium (6 to 12 lbs), Large (13 lbs and up).
- Dogs - Small (up to 20 pounds), Medium (21 to 50 lbs) and Large (51 lbs and up).

While the pet collar product labels recommend trimming of the pet collar after it is applied to the animal, since the handler would be exposed to the full length of the collar during application, trimming of the collar was not accounted for in the residential handler exposure calculations.

Pet Collar Formulation: Per EPA's 2012 Residential SOPs[21], pet collar products are categorized as a liquid formulation (i.e., using inputs and assumptions reflective of liquid formulations). However, in NRDC's Petition related to TCVP pet uses, the NRDC asserted that EPA incorrectly considered the TCVP pet collar formulation to be a liquid formulated product noting that a label for a TCVP pet collar product states that "as the collar begins to work, a fine white powder will appear on the surface." HED reviewed this information and agreed that exposure to the active ingredient as a dust/solid formulation could occur. Due to the uncertainty associated with pet collar formulation type, and without chemical-specific data, HED typically assumes a range of ratios to cover the range of potential exposures (e.g., 1/99, 50/50, and 99/1 liquid/dust). This is consistent with the approach taken for TCVP in the 2016 Occupational and Residential Exposure (ORE) assessment.[22] Since that assessment, a TCVP-specific dust torsion study was submitted and reviewed (MRID 50931601[23]). This study provides a refinement related to the ratio of liquid/dust and provides an estimate of how much TCVP may be released from the collar in the form of a dust/solid. In this study, the weight difference of collar pieces before and after the torsion tests (which involved mechanical torsion and stress by twisting and pulling the collar three times) was measured. This weight difference was assumed to represent the amount of TCVP lost from the collar in the form of dust. Based on the results of this study, EPA determined that 0.38% mass (assumed to be dust) is lost from the collar due to torsional stress. Therefore, in the current exposure and risk calculations for TCVP pet collars, HED assumed a liquid/dust ratio of 99.62/0.38 (i.e., the estimated dose from exposure to a pet collar is calculated for liquids and dusts separately, and then the doses are adjusted by the ratio and added together).

Unit Exposures for all Pet Uses:

Dust/Powders: Chemical-specific unit exposure data were provided in support of the residential handler risk assessment for the dust/powder formulations only (MRID 45519601).

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[21] Available at http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

[22] Available at https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0316-0054

[23] MRID 50931601. D454190. Submitted in response to GDCI-083702-1791.

The study, "*Determination of Dermal and Inhalation Exposures to Tetrachlorovinphos (TCVP) During the Application of an Insecticide Powder to a Dog*," was previously reviewed by the Agency in January 2002 and determined to be acceptable, and the data were reflected in the TRED for TCVP in 2002. These exposure data were used to estimate handler exposures from the TCVP dust/powder products. The study resulted in average unit exposures for the dermal and inhalation routes of exposure of 1,700 mg/lb a.i. and 3.1 mg/lb a.i., respectively.

Liquid Sprays: In the absence of chemical-specific exposure data for residential handling of liquid sprays, the Agency used exposure values from the 2012 Residential SOPs as a surrogate to estimate handler exposures. Surrogate exposure data for a groomer trigger pump spray application to dogs was used to estimate handler exposures from TCVP pump spray products.

Pet Collars: No chemical-specific exposure data are available for assessment of handler exposures from the application of collars. For the liquid portion of the pet collar, the liquid-specific unit exposure (UE) values (i.e., surrogate data from a spot-on applicator study) from the 2012 Residential SOPs[24] were used. For the dust portion of the pet collar, HED used a TCVP dust/powder applicator exposure study (MRID 45519601). The handler doses were then adjusted by the ratio obtained from the torsion study (99.62 liquid/0.38 dust). The liquid formulation spot-on surrogate UE data assumes negligible inhalation exposure; therefore, only the dust-specific UE data (i.e., a TCVP dust/powder applicator exposure study) are expected to result in the potential for inhalation exposures.

Amount Handled: Per the Agency's 2012 Standard Operating Procedures (SOPs) for Residential Pesticide Exposure Assessment,[25] it is assumed that residential handlers of pet treatment products will treat two animals per application.

Exposure Duration: Residential handler exposure is expected to be short-term in duration. Intermediate- and long-term exposures are not likely because of the intermittent nature of applications by homeowners. However, because of the steady state AChE inhibition exhibited by the OPs, steady state exposures (typically 21 days and longer for OPs, but 1 day for TCVP) were assessed and presented for residential exposures to TCVP pet products.

Days per Year of Exposure: For the purpose of assessing residential handler cancer exposure/risk from TCVP product application, EPA has assumed four days per year for collars, and six days per year for dusts/powders and liquid sprays. The collar is based on a worst-case assumption of a single application every three months. Collar re-treatment intervals range from three to seven months. EPA assumed a bi-monthly re-treatment interval for dusts/powders and liquid sprays.

Years per Lifetime of Exposure and Lifetime Expectancy: It is assumed that residential handler exposure would occur for 50 years out of a 78-year lifespan. This factor is routinely

[24]Available at https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

[25] Available at https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

used as a conservative estimate of the number of years an individual could continually use a single pesticide product. Life expectancy values are from the Exposure Factors Handbook 2011 Edition Table 18-1.[26] The table shows that the overall life expectancy is 78 years based on life expectancy data from 2007. In 2007, the average life expectancy for males was 75 years and 80 years for females. Based on the available data, the recommended value for use in cancer risk assessments is 78 years.

2. Residential Handler Risk Estimates and Conclusions

EPA concluded that residential handler (adults) steady state inhalation exposures are not of concern to the Agency (i.e., all margins of exposure (MOEs) are greater than the LOC of 300) from application of any registered TCVP pet products. A complete listing of all MOEs can be found in Tables C.2 and C.3 of the 2020 revised residential exposure assessment.

Estimated residential handler cancer risk estimates range from 10^{-9} to 10^{-7}, which are below the Agency's LOC. A complete listing of all residential handler cancer exposure and risk estimates can be found in Tables D.1 and D.2 in the 2020 revised residential exposure assessment.

C. Residential Post-Application Exposure

In the revised residential exposure assessment, EPA identified that there is the potential for post-application exposure for individuals exposed as a result of contacting a cat or dog previously treated with TCVP pet products. A steady state non-cancer residential post-application exposure assessment (incidental oral only (i.e., hand-to-mouth exposure); no dermal POD selected) was performed for individuals coming into contact with treated cats and dogs. Since there is no non-cancer dermal hazard for TCVP, a quantitative non-cancer post-application dermal exposure assessment was not performed for adults or children. Residential post-application inhalation exposure is expected to be negligible from TCVP pet products and, thus, a quantitative assessment was not performed. Per the Residential SOPs, the combination of low vapor pressure (2.6×10^{-7} mmHg at 25°C) and the small amounts of pesticide applied to pets is expected to result in negligible levels of chemical in the air, and therefore negligible inhalation exposures. In addition, a residential post-application cancer assessment was conducted due to TCVP being classified as a Group C possible human carcinogen by the Agency with a linear low-dose approach for quantification of risk using the oral slope factor (Q1*) of 1.83×10^{-3} $(mg/kg/day)^{-1}$.

1. Residential Post-application Assumptions and Inputs

Application Rate for all Pet Uses: For pet collars, the label directs users to cut off and dispose of any excess length once the product is fit according to directions and buckled into place. Per the 2012 Residential SOP, the full length of the collar is assumed in pet collar assessments, since the exact length that is cut off cannot be determined; therefore, the corresponding active ingredient (a.i.) loss cannot be quantified. In the previous assessment,

[26] Available at https://www.epa.gov/sites/production/files/2015-09/documents/efh-chapter18.pdf

HED assessed the TCVP pet collars assuming the full collar length. Since that time, the registrant has submitted pet collar efficacy data to address this uncertainty. The data provided (from MRID 51079501[27]) is from a 7-month efficacy study in dogs. A total of 63 dogs (range in weights of 11 to 22 kg) were included in the data summary, and the weights of the collars were provided, including the pre-cut weight, the weight of the cut-off piece, and the weight of the fitted collar. The percent of collar removed was calculated by taking the weight of the cut-off piece and dividing by the weight of the pre-cut collar. The percent of the collar removed ranged from 20% to 43%, with an average of 30% being removed. In order to provide a conservative assumption of how much collar might be removed during use, HED has chosen to use a value of 20% to adjust the application rate for pet collars. Accounting for the percentage of the pet collar removed is believed to better represent typical usage of the product as it is fit to the treated animal.

Pet Contact: For the purpose of determining exposure to treated pets, the 2012 Residential SOPs make use of transfer coefficients (TCs). TC is an exposure rate for a selected activity which involves contact with a source, such as children playing with treated pets or on treated turf. The TC concept is a long-standing established approach used to estimate residential, as well as occupational exposures, and is the basis for the Agency's post-application exposure guidelines.[28] A TC is derived by taking the ratio of study volunteer dermal exposure per unit time (mg/hr), and the concurrent measure of residue transfer. Ideally, dermal exposure is based on activities representative of the use pattern, and residue transfer is determined by use of an established method specific to the use pattern. For pet exposures, TCs can be defined as animal surface area contact per unit time (cm^2/hr).

Currently, there is no exposure study available using typical adult and child activities with pets and a concurrent transferable residue (TR) measure. As noted in the 2012 Residential SOPs[29], in the absence of direct exposure data for residential activities with pets, the Agency concluded that studies conducted to monitor pet grooming activities are likely to result in a highly protective estimate of pet contact relative to contact associated with petting, hugging, or sleeping with a pesticide-treated pet since these individuals directly handled pesticide products and had direct contact with treated pets. These pet grooming exposure studies have been submitted to the Agency, reviewed and determined to be acceptable for risk assessment. The data were gathered while human volunteers applied dust/powders and shampoo products to various dogs of differing sizes and fur lengths. Since these individuals extensively handled the dogs, it is expected that their resulting exposures are higher than would be reasonably anticipated from routine contact with treated pets. The volunteers in the shampoo study, who were professional groomers, shampooed 8 dogs for 5 minutes each, rinsed, and lifted them to counters for drying and combing resulting in very high exposures. In the dust study, volunteers applied dust via shaker can to 8 dogs each and then rubbed the dusts into the dogs' coats. The applicator studies were not conducted in a manner which measured TR, or active ingredient per surface area. Therefore, the residue available on the animal for transfer was predicted by multiplying the

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[27] MRID 51079501. *Efficacy and Repellence of Ectoparsiticidal Treatments Against Ticks (Dermacentor Variabilis, Ixodes Scapularis, Rhipicephaslus Sanguineus), Fleas (Ctenocephalides Felis) and Mosquitos (Aedes Aegypti) on Dogs*. May 7, 2019. Table 4 (p. 37 – 39).

[28] Available at http://www.ecfr.gov/cgi-bin/text-idx?SID=6bfd4539761be8d5b20dfbf6bc19b9d0&node=40:25.0.1.1.9.9&rgn=div6

[29] https://www.epa.gov/sites/production/files/2015-08/documents/usepa-opp-hed_residential_sops_oct2012.pdf

arithmetic mean fraction of application rate from the analysis of all liquid formulated product data sets presented in the 2012 Residential SOPs, 0.96%. This approach has the effect of increasing TC estimates, thus resulting in TC values which are more protective of human health. Furthermore, the selection of the mean value, in lieu of the screening level fraction application rate (F_{AR}) value, 2%, further increases the TC estimates with use of the dust and shampoo studies.

Exposure Time: The exposure time (ET) assumption used to assess residential post-application exposure to TCVP pet products is based on the 2012 Residential SOPs. The value is derived from a study which sought to evaluate the times that individuals spend performing different activities around the home. Based upon the 2012 Residential SOPs, the point estimates recommended for adult and child ET with pets are 0.77 and 1 hours, respectively. In the study, animal care is defined as "care of household pets including activities with pets, playing with the dog, walking the dog and caring for pets of relatives, and friends." The data identified the time spent with an animal while performing household activities as recorded in 24-hour diaries by study volunteers. While the activities defined do not necessarily represent the time volunteers were actively engaged in constant contact with the animal as is implicit in the post-application dermal and incidental oral algorithms, the data are the most accurate representation of time spent with pets available and, therefore, it is assumed that contact is continual throughout the timed activity. The Agency assumes the ET value reflects a reasonable high-end estimate of time spent in contact with a dog treated with TCVP pet products.

When use of the study data are coupled with high-end assumptions of pet contact, the result is an exposure assessment that inherently implies vigorous, continual contact for the entire duration of contact. While it is possible that an adult or child may be in close contact with a pet intermittently throughout the day, they would not be actively engaged in the highly vigorous contact implied by use of the TCs based on the applicator exposure data for the full exposure duration assumed. Further, it is possible that adults or children may be exposed from sleeping with a treated pet; however, they are not actively engaged in a high level of contact, or the repeated mouthing behaviors exhibited by children during waking hours, which are inherently assumed in the assessment conducted.

Pet Collar Formulation Type Approach: As was mentioned above for residential handlers, in the current exposure and risk calculations for TCVP pet collars, HED assumed a liquid/dust ratio of 99.62/0.38. For the residential post-application exposure assessment, the Agency used transfer coefficients (dermal exposures) and the fraction of active ingredient on hands from the transfer coefficent studies (hand-to-mouth exposures) specific to both liquid and solid formulation types when assessing pet collar exposures. As was done for residential handlers, the estimated post-application dose from exposure to a pet collar is calculated for liquids and dusts separately, and then the doses are adjusted by the appropriate ratio and added together.

Transfer Data for the Non-Cancer Assessment: Chemical-specific residue transfer studies were used for assessment of post-application exposures from registered TCVP pet products. For dust/powder products and liquid sprays, HED relied on a TCVP powder and pump spray study (MRID 45485501). In 2014, in support of the Agency's response to the NRDC Petition, the

study was reevaluated based on current standards of conduct for pet residue transfer studies.[30] For the purposes of the non-cancer assessment, the transferable residue from the day of application (Day 0) was used as follows: 0.048% (maximum observed) for dusts/powders and 0.81% for liquid sprays (maximum observed).

For pet collars, HED has used two TCVP-specific residue transfer studies. The first is a literature study[31] (Davis et al), which was used previously, and the second is a newly submitted TCVP pet collar study (MRID 50881801[32]). In the previous TCVP risk assessment, a transfer factor of 0.3% (based on a study conducted for 12 days) was used from the Davis study for the non-cancer assessment, which reflected the potential transfer of residues to gloved hands after individuals continuously rubbed for five minutes over the neck of a dog including across the collar and along the tail region. After subsequent review of the methodology used to collect the residues, HED determined that this approach (rubbing continuously over the neck/collar) would likely result in an overestimate of transferable residue because of the repeated intentional high level of contact with the collars. As a result, the transfer factor was revised to reflect the potential transfer of residues after individuals continuously rubbed for five minutes over the neck of the dog with the collar removed for sampling (see further description below) and along the tail region which reduced the factor to 0.17%. This value closely aligns with the value identified from the newly submitted TCVP pet collar residue transfer study which was conducted according to current practice for generating these types of data (i.e., with petting strokes conducted on the right side, on the left side, and along the back line of the dog).

Davis Study Residue Transfer Factor: In the previous risk assessment for TCVP, it was noted that the petting/rubbing method used in this study was not conducted based entirely upon current practice for studies of this type; however, the methodology was relevant for the time at which it was conducted, and it was deemed adequate for risk quantitation. Upon comparison of the Davis study data and the recently submitted TCVP transfer study (which was conducted according to current practice), HED reevaluated the methodology used in the Davis study; specifically, the information provided in the literature study regarding how the petting simulations were conducted. The study authors describe that dogs were petted by volunteers *continuously for a five-minute period* with cotton gloves. Transferable residue (petting/rubbing) samples were collected 1) from the fur of the neck (after application of the collar and rubbing over the collar), 2) from the fur of the neck (after application of the collar and then removal of the collar for sampling), and 3) along the back in the tail region after application of the collar, during two studies; the first study was conducted for 112 days and the second study was conducted for 12 days. Dogs wore the collars continuously throughout the study, but on sampling days, residue transfer was determined with continuous petting over the neck with the collars present for 5 minutes, and then continuous petting over the neck with the collars removed for 5 minutes. Collars were placed back on the dogs after each sampling event.

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[30] Britton, W. 2014. Tetrachlorvinphos: Reevaluation of "HED's Review of *Determination of the Dislodgeability of Tetrachlorvinphos (TCVP) from the Fur of Dogs Following the Application of an Insecticide Powder, Pump Spray or Aerosol*; MRID 45485501. 5/16/14. D420285.

[31] Davis, M. et. al., *Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos*. Journal of Exposure Science and Environmental Epidemiology. (2008) 18, 564-57). D430707

[32] D453149. TCVP: Review and Summary of Residue Transfer Studies Submitted. MRID 50881801.

In the previous risk assessment, HED had relied on residues collected in the Davis study from the fur of the neck (after application of the collar and rubbing over the collar) and from the tail region. The transferable residues collected from the fur of the neck (after application of the collar and then removal of the collar for sampling) were not included since it was thought that the collection of those residues was not consistent with the current practice for pet fur transfer residue studies. Current practice involves petting over the pet collar, assuming that the pet collar is secured in place as directed by product labeling. However, while the petting strokes should not take into account the location of the collar (i.e., the petting should not intentionally avoid the collar), they should begin from the head/neck and end at the tail (i.e., the petting stroke should not be limited to just over the neck and collar in the head/neck area). Therefore, it has been determined that the sampling in the Davis study that involved continuous rubbing over the neck and collar for five minutes likely overestimated the potential transferable residue from typical contact with a pet or what would be expected to be measured following current practice. HED has determined that the residues collected from the fur of the neck (after application and then removal of the collar for sampling) likely do not underestimate exposure considering the continuous rubbing methodology that was followed. Therefore, for the current exposure assessment for pet collars, HED has updated the calculation of the fraction transferred value by dividing the sum of the residues measured from the fur of the neck (after application of the collar and then removal of the collar for sampling) and from the back in the tail region by the amount of active ingredient in the pet collar (as reported in the Davis study), 4,800 mg. The fraction transferred proposed for non-cancer post-application risk assessment, therefore, is 0.0017 (0.17%), and is based on the mean residues reported from the 12 day study [where (8 mg + 0.08 mg)/ 4,800 mg = 0.0017]. Upon reevaluation, HED has determined that the Davis study fraction transferred and the fraction transferred determined from MRID 50881801 transfer study (described below) are similar.

MRID 50881801 Residue Transfer Factor: The Hartz Mountain Corporation submitted a TCVP-specific residue transfer study for pet collars in 2019 (MRID 50881801). The purpose of the study was to measure the transferability of the test substance, TCVP, from the hair of a dog wearing a TCVP-impregnated collar. Each collar contained 14.55% TCVP (TCVP wt/collar wt). A total of 9 dogs were used in the study, randomly assigned to 3 groups. Dogs in Group 1 were petted for 5 simulations, dogs in Group 2 received 10 petting simulations, and dogs in Group 3 received 25 petting simulations. Each simulation consisted of three strokes conducted using a mannequin hand fitted with three cotton gloves. The first stroke was on the right side, the second on the left side, and the third was along the back line. Percent transferable residues of TCVP were calculated by taking the ratio of the residues of TCVP observed on the glove to the total amount of TCVP in the collar at application (calculated as the percent TCVP * initial weight of collar). This resulted in percent transfer values ranging from 0.049% to 0.228%. The average percent transferable residues of TCVP were 0.098% for Group 1 (5 petting simulations), 0.086% for Group 2 (10 petting simulations), and 0.167% for Group 3 (25 petting simulations). For the purpose of non-cancer post-application risk assessment, only the results from group 3 were used since that group used 25 petting simulations, which most closely compares with the current methodology recommendation, which is 20 petting simulations.

Since both studies are representative of potential exposure to currently registered TCVP pet collars and provide similar estimates of transferable residue, the risk estimates presented are representative of both data sets.

Exposure Duration: Residential post-application exposure is expected to be short- and intermediate-term for dust/powders and liquid sprays. For pet collars, post-application exposures are expected to be long-term (greater than 6 months) due to the potential for extended usage in more temperate parts of the country, and the longer active lifetime of pet collar products. Again, because of the steady state AChE inhibition exhibited by the OPs, steady state exposures (typically 21 days and longer for OPs, but 1 day for TCVP) were assessed and presented for residential exposures to TCVP pet products.

Transfer Data for the Cancer Assessment: For purpose of quantification of estimated TCVP post-application cancer exposures/risks, HED used the average percent residue transfer from the TCVP dust/powder and liquid spray studies. HED used an average of the maximum observed percent residue transfer for each day tested for calculation of cancer exposures/risks resulting in a fraction transferred of 0.022% and 0.18% for dusts/powders and liquid sprays, respectively.

For the assessment of pet collar cancer post-application risks, longer-term residue transfer values from the Davis study (112 days) were used to best represent the assumption of 180 days/year exposure for cancer assessment. As noted above for the non-cancer estimate, HED had previously included the residues from the fur of the neck with the collar present in the calculation of the fraction transferred. Updated calculations of the fraction transferred used for cancer post-application risk assessment was also conducted, resulting in a revised fraction transferred of 0.00092 (0.09%), which is based on the mean residues (112 days) reported from the Davis study [where (4.3 mg + 0.13)/ 4,800 mg = 0.00092].

Days per Year of Exposure: For the purpose of estimating adult dermal cancer risks, exposure was assumed for 180 of 365 total days per year. This factor is used as a health protective estimate of the number of days that an individual could be exposed to a treated animal per year of product use. The recommendation of 6 months exposure is conservative, particularly when paired with the assumption that this exposure duration is repeated for 50 years during an adult's lifetime.

Years Per Lifetime of Exposure and Lifetime Expectancy: It is assumed that residential post-application exposure would occur for 50 years out of a 78-year lifespan. This factor is routinely used as a conservative estimate of the number of years an individual could continually use a single pesticide product. Life expectancy values are from the Exposure Factors Handbook 2011 Edition Table 18-1.[33] The table shows that the overall life expectancy is 78 years based on life expectancy data from 2007. In 2007, the average life expectancy for males was 75 years and 80 years for females. Based on the available data, the recommended value for use in cancer risk assessments is 78 years.

[33] Available at https://www.epa.gov/sites/production/files/2015-09/documents/efh-chapter18.pdf

2. Residential Post-application Risk Estimates and Conclusions

Before consideration of the recent requests for registration amendments, some of the current TCVP pet uses result in residential post-application incidental oral exposures for children 1 to <2 years old that are of concern to the Agency (i.e., some MOEs are less than the LOC of 1000).

Liquid Spray Products – EPA has determined that all residential post-application exposures resulting from liquid spray products are not of concern because the MOEs range from 1,600 to 15,000, well above the LOC of 1000. Residential post-application cancer risks estimated for TCVP liquid sprays are all 10^{-7} and are not of concern.

Dust/Powder Products – EPA has determined that all of the dust/powder products have residential post-application risks of concern because the MOEs range from 98 to 640. These are all below the LOC of 1000. Residential post-application cancer risks estimated for TCVP dust/powder products range from 10^{-7} to 10^{-6} and are not of concern.

Pet Collars – EPA has determined that certain pet collar products have risks of concern for certain size animals because the MOEs range from 340 to 2,300 (LOC = 1000). Residential post-application cancer risks estimated for TCVP pet collar products range from 10^{-7} to 10^{-6} and are not of concern.

A complete listing of all MOEs can be found in Tables E.2 and E.3 in the 2020 residential assessment. A complete listing of all residential post-application cancer exposure and risk estimates can be found in Tables F.1 and F.2 in the 2020 revised residential exposure assessment.

It should also be noted that the evaluation of the potential residential post-application health risks from exposures to cats and dogs treated with TCVP pet products is conservative. The risk estimates calculated are based upon protective assumptions of TCVP hazard, product application rates, durations of exposure, and contact with the treated animal, and they make use of the best available post-application exposure data.

A summary of the residential risk estimates resulting from the registered TCVP pet products is provided in the table below. For a more detailed explanation of residential exposure from the use of pet products containing TCVP and the Agency's conclusions, please refer to the 2020 revised residential exposure assessment, entitled *Tetrachlorvinphos: Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses* and the addendum "*Tetrachlorvinphos: Addendum to the Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses*".[34]

[34] Available at https://www.regulations.gov/docket?D=EPA-HQ-OPP-2008-0316 and in Attachment B and C of this document.

Table 1: Summary of TCVP Pet Product Residential Risk Estimates (pre-mitigation)					
Reg. No. (Target Animal)	Size of Animal	Residential Handler Non-cancer MOEs (LOC = 300)	Residential Handler Cancer Risk Estimates	Residential Post-application MOEs[1] (LOC = 1000)	Residential Post-application Cancer Risk Estimates
Pet Collars					
2596-49 (Cat)	Small	1,100,000	1.6E-08	**750**	2.9E-06
	Medium			1,300	1.7E-06
	Large			2,000	1.1E-06
2596-50, 62 (Dog)	Small	630,000	2.7E-08	**900**	2.4E-06
	Large	370,000	4.6E-08	2,000	1.1E-06
2596-63 (Cat)	Small	800,000	2.2E-08	**570**	3.8E-06
	Large	700,000	2.5E-08	1,300	1.6E-06
2596-83 (Cat)	Small	990,000	1.7E-08	**710**	3.0E-06
	Medium	640,000	2.7E-08	**770**	2.8E-06
	Large	480,000	3.6E-08	**910**	2.4E-06
2596-84 (Dog)	Small	630,000	2.8E-08	**900**	2.4E-06
	Large	370,000	4.6E-08	2,000	1.1E-06
2596-139 (Cat)	Small	1,200,000	1.4E-08	**850**	2.5E-06
	Medium			1,400	1.5E-06
	Large			2,300	9.5E-07
2596-139 (Dog)	Small	240,000	7.2E-08	**340**	6.3E-06
	Medium			**790**	2.7E-06
	Large			1,200	1.7E-06
Application of TCVP Dusts/Powders					
47000-123 (Dog)	Small	39,000	3.5E-08	**320**	1.1E-06
	Medium	16,000	8.7E-08	**300**	1.2E-06
	Large	9,700	1.4E-07	**300**	1.2E-06
47000-123 (Cat)	Small	160,000	8.7E-09	**640**	5.4E-07
	Medium	65,000	2.1E-08	**450**	7.8E-07
	Large	43,000	3.1E-08	**480**	7.3E-07
2596-78 (Cat)	Small	24,000	5.7E-08	**98**	3.6E-06
	Large	14,000	9.6E-08	**160**	2.2E-06
2596-79 (Dog)	Small	14,000	9.6E-08	**120**	3.0E-06
	Medium	7,100	1.9E-07	**140**	2.5E-06
	Large	5,600	2.4E-07	**170**	2.0E-06
Application of TCVP Liquid Sprays					
2596-126, -140 (Cat) (Trigger)	Small	25,000	2.5E-08	1,600	9.6E-07
	Large	18,000	3.5E-08	3,100	5.1E-07
2596-140 (Cat) (Pump)	Small	120,000	5.1E-09	8,000	2.0E-07
	Large	87,000	7.2E-09	15,000	1.0E-07
	Small	18,000	3.5E-08	2,300	6.7E-07
	Medium	16,000	4.0E-08	4,800	3.3E-07

Table 1: Summary of TCVP Pet Product Residential Risk Estimates (pre-mitigation)					
Reg. No. (Target Animal)	Size of Animal	Residential Handler Non-cancer MOEs (LOC = 300)	Residential Handler Cancer Risk Estimates	Residential Post-application MOEs[1] (LOC = 1000)	Residential Post-application Cancer Risk Estimates
2596-125, -140 (Dog) (Trigger)	Large	8,900	7.0E-08	4,300	3.7E-07

1. Bolded values indicate MOEs that are of concern because they are below the LOC of 1000.

For those pet collars that had resulted in post-application risk estimates of concern, the registrant provided registration amendments to address those risk concerns. Those amendments involved either (1) cancelling certain pet collar products, (2) adding a weight restriction to the pet collar product labels (i.e., cats and kittens must weigh at least 5 pounds), and/or (3) a redesign of the pet collars. Based on the registration amendments, the post-application MOEs will not be of concern (i.e., all MOEs are ≥ 1000).

A summary of the residential risk estimates after consideration of the proposed registration amendments for the TCVP pet products is provided in the table below. A complete listing of the updated residential non-cancer and cancer risk estimates for pet collars post-mitigation can be found in Table 1 of the 2020 Addendum ("*Tetrachlorvinphos: Addendum to the Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses*").[35]

Table 2: Summary of TCVP Pet Product Residential Risk Estimates (post-mitigation)					
Reg. No. (Target Animal)	Size of Animal	Residential Handler Non-cancer MOEs (LOC = 300)	Residential Handler Cancer Risk Estimates	Residential Post-application MOEs (LOC = 1000)	Residential Post-application Cancer Risk Estimates
Pet Collars					
2596-49 (Cat)	Medium	1,100,000	1.6E-08	1,300	1.7E-06
	Large			2,000	1.1E-06
2596-50, 62 (Dog)	Small	900,000	1.9E-08	1,300	1.7E-06
	Large	500,000	3.4E-08	2,600	8.2E-07
2596-83 (Cat)	Medium	1,200,000	1.4E-08	1,500	1.6E-06
	Large	900,000	1.9E-08	1,700	1.3E-06
2596-84 (Dog)	Small	900,000	1.9E-08	1,300	1.7E-06
	Large	500,000	3.4E-08	2,600	8.2E-07
2596-139 (Cat)	Medium	1,200,000	1.4E-08	1,500	1.6E-06
	Large	900,000	1.9E-08	1,700	1.3E-06

[35] Available at https://www.regulations.gov/docket?D=EPA-HQ-OPP-2008-0316 and in Attachment C of this document.

Table 2: Summary of TCVP Pet Product Residential Risk Estimates (post-mitigation)					
Reg. No. (Target Animal)	Size of Animal	Residential Handler Non-cancer MOEs (LOC = 300)	Residential Handler Cancer Risk Estimates	Residential Post-application MOEs (LOC = 1000)	Residential Post-application Cancer Risk Estimates
2596-139 (Dog)	Small	900,000	1.9E-08	1,300	1.7E-06
	Medium	650,000	2.7E-08	2,200	1.0E-06
	Large	500,000	3.4E-08	2,600	8.2E-07
Application of TCVP Liquid Sprays					
2596-126, -140 (Cat) (Trigger)	Small	25,000	2.5E-08	1,600	9.6E-07
	Large	18,000	3.5E-08	3,100	5.1E-07
2596-140 (Cat) (Pump)	Small	120,000	5.1E-09	8,000	2.0E-07
	Large	87,000	7.2E-09	15,000	1.0E-07
2596-125, -140 (Dog) (Trigger)	Small	18,000	3.5E-08	2,300	6.7E-07
	Medium	16,000	4.0E-08	4,800	3.3E-07
	Large	8,900	7.0E-08	4,300	3.7E-07

IV. Benefits and Impact Assessment of Cancellation of Dust Products and Select Collars

In considering the Petition to cancel TCVP pet products (dusts, collars, and liquid sprays), EPA assessed the benefits of TCVP pet collars, considering the availability of other pet products.[36] EPA also considered the importance of TCVP dust and powder products in the control of pests that infest pets.

Pet Insecticide Usage

Based on available private market research, shown in Table 1, sales of consumer market pet insecticides in 2016 were approximately $1.5 billion, a 25 percent increase over sales in 2011 of $1.2 billion, unadjusted for inflation.[37] In 2016, the top pet insecticide formulation, in terms of sales, was liquid products, which represented more than 80 percent of the market as shown in the table below, followed by tablets for veterinary use with 12.7 percent of sales.[38] As a proportion of sales, collars have remained similar over time (Table 3). As discussed below, collars tend to be cheaper and provide longer-lasting control than liquid sprays and dusts and powders. Therefore, the proportion of sales does not represent the proportion of usage. Expenditures on dust and powder formulations declined in nominal terms from 2011 to 2016, which likely indicates a decrease in usage.

[36] Atwood, D., and S. Smearman. 2017. Alternatives Assessment for Tetrachlorvinphos (TCVP) (PC Code 083702) Impregnated Flea and Tick Collars on Dogs and Cats. Available at https://www.regulations.gov/docket?D=EPA-HQ-OPP-2008-0316.

[37] Non-Agricultural Market Research (Proprietary) Data. 2016. Studies conducted and sold by a consulting and research firm. Report on consumer pesticide usage. [Accessed June 2020.]

[38] *Ibid*

Table 3. Sales of Pet Products, by Formulation

Product Form	2011		2016	
	$ million	percent	$ million	percent
Liquids [1]	949.7	78.0	1,188.9	80.7
Tablets [2]	182.6	15.0	187.1	12.7
Collars	60.9	5.0	98.7	4.6
Dusts and Powders	12.2	1.0	7.3	0.5
Other (aerosols, foggers, soaps, combs, & traps)	12.2	1.0	21.5	1.5
Total	1,217.5		1,473.4	

Source: Kline and Company. 2012. Consumer Markets for Pesticides and Fertilizers 2011. [Accessed June 2020.]; Non-Agricultural Market Research Proprietary Data. 2016. Studies conducted and sold by a consulting and research firm. Report on consumer pesticide usage. [Accessed June 2020.]

[1] Includes shampoos, dips, and topical spot-ons.

[2] Veterinary supplied oral treatments.

Based on preliminary private market research of sales of brands carrying the TCVP flea collars, sales were estimated to be slightly more than 50 percent of the total pet collar sales in the U.S. in 2018 (NMRD, 2019; Personal communication with C. Doucoure, Email dated 6/11/2020, may contain CBI). During the same period, TCVP flea powder sales based on the Hartz Flea and Tick Powder were estimated to be between $3 to $5 million. Thus, based on 2016 sales figures, TCVP products likely account for a majority of the usage of powder and dust products.

Dust Products

Pyrethrins, phenothrin and permethrin are the only active ingredient alternatives to TCVP available for control of arthropod pests of pets in dust formulations. TCVP dust products provide control of fleas, ticks, sarcoptic mange mites and lice on pets and pet bedding. The labels recommend repeating the application weekly and at a minimum of three treatments for control of fleas, ticks, and lice. Label recommendations for sarcoptic mange mites differ slightly in that application may be applied more frequently. According to several sources, including TCVP dust product labels, veterinary consultation is always recommended when dealing with mange mites and resulting infections, and since veterinary sources do not identify TCVP as a recommended treatment method, EPA concludes that TCVP likely does not play a major role in the market for treatments of sarcoptic mange mite infestations in cats and dogs (e.g., EPA Reg No. 2596-79; Ward and Panning, 2017; Veterinary Manuel, 2020).

Numerous other insecticide formulations (i.e., EPA registered insecticide-impregnated pet collars, pesticidal shampoos, sprays, dips, spot-ons, and treatments regulated by Food and Drug Administration) are available for control of pests on pets. Among pet products, TCVP dusts would likely be considered a product for curative use that offers some limited residual benefit (labeled for 1-week control or less). Products providing similar immediate control of current infestation of these pests would be sprays, shampoos and veterinarian-prescribed medications which may include shampoos or various other topical and feed-through treatments.

However, other products such as impregnated collars and spot-on treatments offer control and prevention of these same pests for a much greater duration (1-7 months control) and thus would be the superior choice for long-term prevention.

TCVP dust products are unique among dust-formulated products for pet-pest control in that they are registered for control of lice and sarcoptic mange; however, several products containing other active ingredients (fipronil, imidacloprid, malathion, etc.) not in dust formulations are available to control these pests. Consumers utilizing TCVP dusts for typical pests such as fleas and ticks can choose the alternate TCVP spray formulations or a dust formulation of phenothrin, permethrin or pyrethrin as previously mentioned. Both dust and spray formulations can be used interchangeably, control the same key pests (fleas and ticks) as TCVP-based dust products and are similar in price. For mange mite and lice treatment, consumers utilizing TCVP dusts would likely turn to other active ingredients in various formulation types. Although several topical and impregnated collar products are registered for control and prevention of lice and the prevention of mange mites for pets, the treatment (as opposed to control) of sarcoptic mange mites may predominantly come from veterinary-prescribed medications which are associated with much greater costs (veterinarian visit, prescription fee, and product cost).

Overall, the Agency expects little long-term impact from the removal of TCVP dust-formulated pet-pest control products given the availability of alternative dust and spray products, including TCVP spray products, that provide similar flea and tick control and ease of use. Users may have to buy more expensive products, but given the competitive nature of the market, prices are likely similar. Cost increases may be greater for users seeking control of mange mites and lice, since suitable over-the-counter products may be less readily available.

Collars

TCVP pet collars are a relatively low cost means of controlling fleas and ticks on companion animals. Alternative control mechanisms include collars formulated with other insecticides; liquid insecticides such as shampoos, sprays, and topical spot-ons; dusts; and veterinary medicines. Most of these products can provide similar levels of control of both fleas and ticks as TCVP collars, although shampoos may not provide long-term control of ticks.[39] Alternative pet collars for dogs and cats mostly contain a combination of flumethrin and imidacloprid. Deltamethrin collars are also available for dogs. There are also several liquid products that would provide similar efficacy, although retreatment is necessary to achieve the duration of control provided by a collar. These products often combine a pyrethroid, or similar chemical, with imidacloprid, indoxacarb, or pyriproxyfen.[40]

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[39] Atwood, D., and S. Smearman. 2017. Alternatives Assessment for Tetrachlorvinphos (TCVP) (PC Code 083702) Impregnated Flea and Tick Collars on Dogs and Cats. Biological and Economic Analysis Division, Office of Pesticide Programs, U.S. EPA. 27 pp. Sept 15. Available at https://www regulations.gov/docket?D=EPA-HQ-OPP-2008-0316.

[40] *Ibid*

Collars tend to provide six to seven months of control. Treatment with liquid products or veterinary medicines may need to be done monthly. A check of prices at several major pest supply stores in 2017 suggests that, converted to monthly costs, TCVP collars tend to be lower cost relative to other products.[41] However, several topical spot-on products containing etofenprox are available that may be within two or three dollars of the TCVP collars and would probably be the most likely alternatives. Spot-on products are less convenient because they must be reapplied about every month. Collars containing other insecticides would be as convenient as TCVP collars but may be $30 to $60 more expensive per collar or five or six dollars more expensive on a monthly basis. Veterinary medicines, which require a prescription, tend to be substantially more expensive as well as less convenient to obtain and use.[42]

There could also be some short-term costs to consumers who rely on known brands and will have to research other products. These costs may be modest. According the American Veterinary Medical Association (AVMA, 2012), over 80 percent of dog owners and nearly 45 percent of cat owners take their pets to the veterinarian at least once per year and the veterinarian would be a ready source of information about pet insecticide products. More than 30 percent of pet owners purchase pet insecticide products from a veterinarian.[43]

If EPA were to cancel all TCVP pet collars, there would likely be some increased costs for consumers, either monetarily due to the higher cost of alternative collars or through additional time and effort required for topical spot-on products.

Impacts on Low Income Consumers

BEAD also assessed whether the lower cost in effort and money of TCVP pet collars and dust products could suggest that, if EPA were to cancel these products, their unavailability could disproportionally affect low income pet owners. BEAD finds that this does not appear to be the case. Usage of pet collars may be somewhat more common among low income households; about 30 percent of pet owners with a family income of less than $25,000 per year used pet collars compared to about 25 percent of pet owners in other income categories.[44]

The usage of dust/powders is somewhat lower, four percent of low-income households reported using dusts and powders compared to six to nine percent of households in higher income groups. Usage of topical spot-ons was similar across income categories with 48 percent of pet owners with income less than $25,000 using spot-ons compared to rates of 47 to 57 percent for other income groups. Overall, usage of pet insecticides is similar for pet owners regardless of income. Seventy-two percent of low-income pet owners reported having used pet insecticides compared to 70 percent of all households.[45]

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[41] Atwood, D., and S. Smearman. 2017. Alternatives Assessment for Tetrachlorvinphos (TCVP) (PC Code 083702) Impregnated Flea and Tick Collars on Dogs and Cats. Biological and Economic Analysis Division, Office of Pesticide Programs, U.S. EPA. 27 pp. Sept 15. Available at https://www regulations.gov/docket?D=EPA-HQ-OPP-2008-0316.

[42] *Ibid*

[43] Kline and Company. 2012. Consumer Markets for Pesticides and Fertilizers 2011. [Accessed June 2020.]

[44] *Ibid*

[45] *Ibid*

If EPA were to remove TCVP dust products and pet collars, there may be some increase in costs for consumers, but it would not disproportionally affect low income pet owners. Other pet pest control options are available that perform comparably to TCVP and it is unlikely that consumers would forego pest treatments due to the increase in costs.

Market Impacts

As noted in the Pet Insecticide Usage section above, TCVP pet collars and powders account for a majority of current sales in those particular segments of the market. An immediate removal of these products could exacerbate what impacts occur due to shortages of alternative products. Demand for flea and tick products may be greatest in the spring and summer months because pests are more active in warmer temperatures and people and their pets may spend more time outdoors.

V. EPA's Responses to NRDC's Petition Claims

A. Statutory Background

1. Pesticide Registration and Registration Review

FIFRA, 7 U.S.C. §§ 136-136y, in general, requires EPA approval of pesticides prior to their distribution or sale, and establishes a registration regime for regulating the use of pesticides. *Id.* FIFRA sections 3(a), 3(c). EPA must approve an application for pesticide registration if, among other things, the pesticide will not cause unreasonable adverse effects on the environment. *Id.* FIFRA section 3(c)(5); *see also id.* FIFRA section 2(bb). When determining whether a pesticide will cause unreasonable adverse effects on human health or the environment, EPA must balance the risks of the pesticide against the benefits of its use. *See* Sections III and IV. Specifically, FIFRA section 2(bb) requires EPA to "[take] into account the economic, social, and environmental costs and benefits of the use of any pesticide." FIFRA section 2(bb). Once a pesticide is registered, EPA cannot unilaterally change the registration without either the registrant requesting an amendment to their registration or EPA taking action under FIFRA section 6 (e.g., initiating cancellation). *See* 40 CFR 152.44.

FIFRA also requires that EPA periodically review registered pesticides. FIFRA section 3(g). The purpose behind registration review is to account for "the rapid development of science and the subsequent application of that knowledge in how it impacts human health and the environment." 70 Fed. Reg. at 40,252. Registration review therefore "establish[es] ongoing scientific look-back procedures" to account for this "continually evolving" landscape. *Id.* at 40,253.

The process EPA uses for evaluating the potential for health and ecological effects of a pesticide is called risk assessment, which is part of a risk management process. In registration review, that risk assessment typically includes an ecological risk assessment, a human health risk assessment, and, when appropriate, a cumulative risk assessment (evaluating the risk of a common toxic effect associated with concurrent exposure by all relevant pathways and routes of exposure to a group of chemicals that share a common mechanism of toxicity). EPA separately

assesses the benefits the chemical provides the users (impacts of the loss of the chemical) and/or the impacts of potential mitigation.

The initial registration review cycle must be completed within 15 years after the first pesticide containing a new active ingredient is registered, but not later than October 1, 2022. *Id.* Registration review does not result in the cancellation of a particular registration. *Id.* FIFRA section 3(g)(1)(A)(v). Instead, if EPA determines that a pesticide does not meet the standard for registration, EPA must comply with the requirements of FIFRA section 6 to proceed to seek cancellation. *Id.* As noted earlier in this response, registration review is currently underway for all TCVP uses.

2. Pesticide Cancellation Process

In relevant part, FIFRA section 6(b) authorizes EPA to initiate cancellation proceedings "[i]f it appears to the [Agency] that a pesticide . . . generally causes unreasonable effects on the environment." EPA can issue a notice of intent to either: (1) cancel the registration; or (2) hold a hearing to decide whether the registration should be cancelled. *Id.* Before issuing such a notice, EPA must consider a series of factors identified in the statute and complete a prescribed process for allowing the Secretary of the Department of Agriculture (USDA) and the FIFRA Scientific Advisory Panel (SAP) (a group of scientists charged with providing EPA with advice related to pesticide actions) to comment on the proposed notice at least 60 days prior to publication. *Id.*; *see also*, *id.* FIFRA section 25(d). Additionally, when a public health use is involved (e.g., flea and tick protection), section 6(b) the Department of Health and Human Services (HHS) should also provide information on the benefits and use or an analysis thereof. Unless they waive review, USDA, HHS, and the SAP may comment during those 60 days. FIFRA sections 6(b) and 25(d). When a draft Notice of Intent to Cancel (NOIC) is based on scientific issues, EPA would expect the SAP to need additional time in order to convene a meeting following the procedures of the Federal Advisory Committee Act. *See* 5 U.S.C. Appendix 2 (1972). EPA needs to address any comments it receives from the SAP or USDA before moving forward to publish the Notice of Intent to Cancel. EPA does not take lightly the steps required for initiating cancellation under FIFRA section 6(b). If any steps are hastily completed and ultimately result in a need to change the program's proposal, it may result in needing to begin the process afresh.

EPA must publish in the Federal Register the proposed NOIC; any comments from the USDA; and EPA's response to such comments. *Id.* FIFRA section 6(b). After the NOIC is issued, the registrant may, within 30 days, request an evidentiary hearing before a hearing examiner (i.e., Administrative Law Judge (ALJ)). FIFRA section 6(d). Once a hearing is requested and an ALJ is appointed, control of the pace of the cancellation proceeding moves from the program office to the Office of the Administrative Law Judges. FIFRA implementing regulations set forth in 40 CFR Part 164 provide specifics on the cancellation process. The hearing is an administrative trial that typically involves exchanges of documents and witness lists. Interested parties other than the registrant can seek intervention. 40 CFR 164.31. Because NRDC filed its Petition requesting cancellation of these uses, it seems highly likely that NRDC would request intervention. Additionally, other trade organizations that represent the registrant industry may also request intervention. Generally, the parties agree to file written testimony from witnesses, who can then be cross-examined by other parties. The ALJ then makes an initial decision based upon the record. Any order to cancel or revise the registration must be "based

only on substantial evidence of record of such hearing and shall set forth detailed findings of fact upon which the order is based." *Id.* FIFRA section 6(d).

Given the many steps of the cancellation process, arriving at an initial order from the ALJ can take a significant amount of time. For instance, in the most recent case where EPA sought cancellation through FIFRA section 6(b), due to pre-hearing motions practice and discovery, a full year had passed between the issuance of the Notice of Intent to Cancel on February 5, 2013 and a pre-hearing order that was issued by the ALJ on February 10, 2014. Resolution through the hearing could have taken much longer, but ultimately the proceeding was dismissed after the registrants agreed to a voluntary cancellation in May of 2014 provided they could continue to sell and distribute the products at issue through March of 2015.[46] Even after the ALJ's decision is issued, the cancellation proceeding may take additional time as it can be appealed by any party to the Environmental Appeals Board (EAB), which, on behalf of the Administrator, issues the final decision for the Agency. A final cancellation order following a public hearing is subject to judicial review within 60 days after entry of the order. Judicial review is only to those adversely affected by the order and who participated as a party in the hearing (EPA cannot appeal an adverse decision). If every appeal opportunity were pursued, a final decision would be years off and the products would remain on the market throughout the proceedings.

In contrast to this adversarial cancellation process, EPA also has the authority to allow registrants to voluntarily cancel their pesticide registrations. Under FIFRA, a registrant can request the voluntary cancellation of a registration pursuant to the procedures in section 6(f). EPA must provide notice and a period for public comment before granting such a request. FIFRA section 6(f)(1). This process takes much less time and fewer resources than cancellation under FIFRA section 6(b). Under FIFRA section 6(f), the registrant requests that EPA either cancel an entire product registration or terminate specific uses on a registration. EPA publishes the request for no less than a 30-day public comment period. Once that comment period is over, EPA may grant or deny the request. If EPA grants the request, it will issue an order either cancelling the registration or terminating certain uses. While the statute provides EPA with discretion to grant or deny any registrant request to voluntarily cancel their product or terminate any use, if a registrant makes such a request, EPA would be unlikely not to grant these requests as a registrant poised to cancel can always make the decision to stop selling or producing any registered pesticide product even if EPA leaves the registration in place.

To cancel pesticide registrations (or terminate uses) by any method under FIFRA section 6, EPA issues a cancellation order. In such cancellation order, EPA has the authority under FIFRA section 6(a) to allow for the sale, distribution, and use of existing stocks of the pesticide product despite it or its terminated use no longer being registered. EPA's issuance of a cancellation order is a separate final Agency action under FIFRA. If there is no public hearing (i.e., public comment period) on the cancellation order, judicial review in in the U.S. district courts as set forth in FIFRA section 16(a).

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[46] Additional information available at https://yosemite.epa.gov/oarm/alj/ALJ_Web_Docket.nsf/Filings-and-Attachments/AD03ABD1E46C104685257D6300739B49/$File/Reckitt_14-08-07_order_on_joint_motion_to_dismiss.pdf ; and https://www.regulations.gov/document?D=EPA-HQ-OPP-2013-0049-0012

B. Rationale for Denying Petition

As summarized above, NRDC's Petition raised several issues, and ultimately requested that EPA cancel all TCVP pet uses. EPA has considered that request to be the true thrust of the Petition and to the extent that the request was for EPA to initiate cancellation proceedings under section 6(b) of FIFRA, that request is denied as explained below product-by-product. But as a preliminary matter, EPA briefly addresses the other issues raised:

- To the extent NRDC's claimed flaws to the 2002 human health risk assessment was a request to revisit EPA's reregistration decision, EPA declines to do so and notes that reregistration has been superseded by registration review. EPA will consider exposures to adults and children from any remaining TCVP pet uses as part of the full TCVP registration review human health risk assessment.
- To NRDC's claims that EPA's previous assessment underestimated exposures to children, including toddlers who are exposed through hand-to-mouth activity, as described above in Section III, EPA has completed a new non-occupational residential exposure assessment for all TCVP pet uses. The assessment addresses potential exposures from hand-to-mouth activity and incorporates new information regarding transferable residues and formulation types.
- To the extent NRDC was requesting that EPA rely on its April 2009 Issue Paper, the Agency continues to not consider this due to the unavailability of the underlying data as described in Section II.C. To the extent NRDC was requesting that EPA rely on the Davis study, the Agency notes that this study was considered in the new non-occupational residential exposure assessment for all TCVP pet uses as described in Section III.

Moving to what EPA considers the thrust of NRDC's request – to initiate cancellation of all TCVP pet uses under FIFRA section 6(b) - EPA's denial of this Petition is based, in part, on agreements between the Agency and the registrants to voluntarily cancel or amend their products or certain uses under FIFRA section 6(f). EPA and the primary registrant of TCVP products with pet uses, Hartz, came to a comprehensive multi-phased agreement to address potential risks of concern identified by the Agency for specific Hartz pet-use products. This package agreement effectuates voluntary cancellations and termination of uses requested by the registrants under FIFRA section 6(f) and amendments to the remaining registrations in a phased approach that will resolve EPA's risk concerns more quickly than an adversarial cancellation proceeding under FIFRA 6(b) could have done. Here, the changes being requested are in response to EPA's determination that there are certain uses that have potential risks of concern. The following sections are divided by pet use type along with EPA's rationale for denying this Petition.

1. Liquid Spray Pet Uses

Taking into consideration all of the information submitted to EPA by the Petitioner and the registrants, and described above in more detail, EPA determined that all of the liquid spray products are not of concern. For these products, the MOEs range from 1,600 to 120,000, which are well above EPA's level of concern of 1000. Because EPA did not find any risks of concerns related to these uses, EPA did not assess the benefits of these products. Therefore, EPA finds that HARTZ 2 IN 1 FLEA AND TICK PUMP FOR DOGS II (EPA Registration No. 2596-

125), HARTZ 2 IN 1 FLEA AND TICK PUMP FOR CATS II (EPA Registration No. 2596-126), and HARTZ RABON SPRAY WITH METHOPRENE PUMP FORMULATION (EPA Registration No. 2596-140) and the pet uses they include meet the FIFRA standard for registration, and EPA denies Petitioner's request to cancel these uses.

2. Dusts and Powder Pet Uses

EPA has determined that all of the dust/powder TCVP pet products have potential risks of concern because the residential post-application MOEs range from 98 to 640 (MOE < the LOC of 1000). The registrants agreed to voluntarily cancel their dust and powder pet products or terminate pet uses. On July 10, 2020, Hartz submitted requests to voluntarily cancel HARTZ 2 IN 1 FLEA AND TICK POWDER FOR CATS (EPA Registration No. 2596-78) and HARTZ 2 IN 1 FLEA AND TICK POWDER FOR DOGS (EPA Registration No. 2596-79).[47] On June 19, 2020, Chem-Tech Ltd. voluntarily submitted a request to terminate cat and dog uses from CLEAN CROP LIVESTOCK 1% RABON DUST (EPA Registration No. 47000-123). The remaining uses on this registration are not pet uses and will be assessed in registration review along with all other uses of TCVP. Consistent with FIFRA section 6(f), EPA will publish these requests in the Federal Register and provide a 30-day public comment period. After reviewing any substantive comments, EPA expects to be able to finalize these requests shortly after the 30-day comment period ends.

As noted above in BEAD's analysis, immediate cessation of the availability of these products could result in harm to those who count on these products during the heart of flea and tick season. Taking this into consideration, EPA believes the request by Hartz to allow for production of these products until July 31, 2020, and sale and distribution of existing stocks until March 31, 2021, is reasonable. Additionally, it is unlikely that EPA could have completed a cancellation proceeding under FIFRA section 6(b) earlier than these dates. As long as EPA is able to grant these requests to terminate these uses or cancel these specific pet products with the allowances for limited production, and sale and distribution, EPA's potential risks of concern will be addressed, and EPA therefore denies Petitioner's request to cancel these uses under FIFRA section 6(b).

[47] A full list of supplemental distribution products is available in Attachment A of this document.

Table 4: Summary of TCVP Dusts/Powders Residential Post-Application Risk Estimates and Mitigation Requirements (Pre-mitigation)				
Reg. No. (Target Animal)	Product Name	Size of Animal	Residential Post-application MOEs (LOC = 1000)	Mitigation Required /Status
47000-123 (Dog)	CLEAN CROP LIVESTOCK 1% RABON DUST	Small	**320**	Registration amendments submitted on June 19, 2020 to remove applications to dogs from product labels (i.e., only livestock uses will remain)
		Medium	**300**	
		Large	**300**	
47000-123 (Cat)		Small	**640**	
		Medium	**450**	
		Large	**480**	
2596-78 (Cat)	HARTZ 2 IN 1 FLEA AND TICK POWDER FOR CATS	Small	**98**	Voluntary cancellation submitted on July 10, 2020
		Large	**160**	
2596-79 (Dog)	HARTZ 2 IN 1 FLEA AND TICK POWDER FOR DOGS	Small	**120**	Voluntary cancellation submitted on July 10, 2020
		Medium	**140**	
		Large	**170**	

3. Pet Collar Uses

EPA has determined that certain pet collar products have potential risks of concern for certain size animals because those MOEs are below the LOC (MOEs < 1000). To address the potential risks of concern, the registrant, Hartz, has agreed to various changes to mitigate the identified issues. With these changes, the risks of concern will be mitigated.

First, on July 10, 2020, Hartz submitted to EPA a request to voluntarily cancel (without condition), under FIFRA section 6(f), HARTZ 2 IN 1 PLUS LONG LASTING COLLAR FOR CATS, EPA Registration No. 2596-63.[48] Consistent with FIFRA section 6(f), EPA will publish this request in the Federal Register and provide a 30-day public comment period. EPA expects to be able to finalize this request shortly after the 30-day comment period ends. After reviewing any substantive comments, as long as EPA is able to grant this request, it is the Agency's intention not to allow any further sale or distribution of this product.

As discussed above, achieving the agreement from the registrant to voluntarily cancel this registration addresses the risks of concern and is much less time consuming than a full cancellation hearing under FIFRA section 6(b). This also results in having a date certain for the

[48] A full list of supplemental distribution products is available in Attachment A of this document.

ending of production and an ending of sale and distribution of this product. EPA therefore denies Petitioner's request to cancel this registration under FIFRA section 6(b).

Second, Hartz agreed to amend HARTZ 2 in 1 COLLAR FOR CATS (EPA Registration No. 2596-49) to limit the use to cats and kittens weighing at least 5 pounds (i.e., the age (currently on the label) and the new weight restriction effectively prohibits use on small cats, which was associated with MOEs that were of concern). With this label restriction, residential post-application MOEs are above 1000. On or about July 1, 2020, EPA received a request from Hartz to amend its label to effectuate this change. EPA expects to review this amendment expeditiously. Hartz also requested that they be allowed to produce this product using the previously approved ("pre-amendment") labels until July 31, 2020. And, they requested that they be allowed to sell or distribute any product "released for shipment" (as that term is defined at 40 CFR 152.3) by July 31, 2020 until March 31, 2021. This change leaves only uses on this registration where the MOEs are equal to or above 1000, therefore not a risk of concern. See Table 5.

As long as EPA is able to grant this request to amend this registration with the allowances for limited production, and sale and distribution, EPA's potential risks of concern will be addressed, and EPA therefore denies Petitioner's request to cancel this product under FIFRA section 6(b). As noted above in BEAD's analysis, immediate cessation of the availability of this product could result in harm to those who count on this product during flea and tick season. Therefore, EPA allowing for limited further production, and sale and distribution provisions, is reasonable.[49]

Third, to address another set of potential pet collar risks of concern identified by EPA, Hartz agreed to amend the products listed below[50] to include a redesign of the collars. EPA has determined that these redesigns would result in MOEs $\geq$ 1000, and therefore no longer present risks of concern.

- HARTZ 2 in 1 COLLAR FOR DOGS, EPA Registration No. 2596-50
- HARTZ 2 IN 1 PLUS LONG LASTING COLLAR FOR DOGS, EPA Registration No. 2596-62
- HARTZ 2 IN 1 PLUS SEVEN MONTH COLLAR FOR DOGS, EPA Registration No 2596-84

These amendments were submitted on or about July 1, 2020 and are currently under review; EPA intends to act expeditiously on them including determining whether the redesigned collars continue to provide appropriate efficacy. In addition to the redesign amendments sent to EPA, consistent with discussions with Hartz, on July 10, 2020, Hartz submitted requests to amend their registrations to memorialize agreements between the Agency and Hartz. EPA expects to approve these amendments quickly. The following is a summary of these provisions. As long as EPA approves the redesign amendments by October 31, 2020, Hartz will cease production of the currently-formulated products no later than February 28, 2021 and will be able to sell and distribute currently-formulated product "released for shipment" (as that term is

[49] A full list of supplemental distribution products is available in Attachment A of this document.
[50] A full list of supplemental distribution products is available in Attachment A of this document.

defined at 40 CFR 152.3) only until May 31, 2021. If EPA does not approve the amendments by October 31, 2020, but does so by December 31, 2020, then the dates for production and sale and distribution of currently-formulated product are extended day-by-day for the time beyond October 31, 2020 EPA needed to approve the amendments. In the unlikely event that EPA will not be able to grant amendments that remove the risks of concern, EPA will take appropriate regulatory action to address these registrations.

As long as EPA is able to grant these requests to amend these registrations with the allowances for limited production, and sale and distribution, EPA's potential risks of concern will be addressed, and EPA therefore denies Petitioner's request to cancel these uses under FIFRA section 6(b). As noted above in BEAD's analysis, immediate cessation of the availability of these products could result in harm to those who count on these products during the heart of flea and tick season. Therefore, EPA allowing for limited further production, and sale and distribution provisions, is reasonable.[51]

Fourth, for the two remaining pet collars with risks of concern identified by EPA, Hartz agreed to amend the products HARTZ 2 IN 1 PLUS SEVEN MONTH COLLAR FOR CATS, EPA Registration No. 2596-83 and HARTZ RABON COLLAR WITH METHOPRENE, EPA Registration No. 2596-139 (cat and dog) to include a redesign of the collars as well as label amendments to limit the use to cats and kittens weighing at least 5 pounds (i.e., the age (currently on the label) and the new weight restriction effectively prohibits use on small cats). EPA has determined that these redesigns would result in MOEs $\geq$ 1000, and therefore would no longer present risks of concern.

The following is a summary of additional registration amendments that Hartz has requested and that EPA expects to approve quickly. As long as EPA can determine that the redesigns continue to provide the appropriate efficacy and EPA approves the redesign and labeling amendments by October 31, 2020, Hartz will cease production of the currently-designed products no later than February 28, 2021 and will be able to sell and distribute currently-designed product "released for shipment" (as that term is defined at 40 CFR 152.3) only until May 31, 2021. If EPA does not approve the amendments by October 31, 2020, but does so by December 31, 2020, then the dates for production and sale and distribution are extended day-by-day for the time beyond October 31, 2020 EPA needed to approve the amendments. In the unlikely event that EPA will not be able to grant amendments that remove the risks of concern, EPA will take appropriate regulatory action to address these registrations.

As long as EPA is able to grant these requests to amend these registrations with the allowances for limited production, and sale and distribution, EPA's potential risks of concern will be addressed, and EPA therefore denies Petitioner's request to cancel these uses under FIFRA section 6(b). As noted above in BEAD's analysis, immediate cessation of the availability of these products could result in harm to those who count on these products during flea and tick season. Therefore, EPA allowing for limited further production, and sale and distribution provisions, is reasonable.[52]

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[51] A full list of supplemental distribution products is available in Attachment A of this document.
[52] A full list of supplemental distribution products is available in Attachment A of this document.

Table 5: Summary of TCVP Pet Collars Residential Post-Application Risk Estimates and Mitigation Requirements					
Reg. No. (Target Animal)	Product Name	Size of Animal	Pre-mitigation Residential Post-application MOEs (LOC = 1000)	Post-mitigation Residential Post-application MOEs (LOC = 1000)	Mitigation Required /Status
2596-49 (Cat)	HARTZ 2 in 1 COLLAR FOR CATS	Small	**750**	**NA***	Amendments submitted on or about July 1, 2020 to restrict use by animal weight, i.e., not for use on small cats (weigh 5 pounds or more)
		Medium	1,300	1,300	
		Large	2,000	2,000	
2596-50 (Dog)	HARTZ 2 in 1 COLLAR FOR DOGS	Small	**900**	1,300	Product formulation amendments submitted on or about July 1, 2020
		Large	2,000	2,600	
2596-62 (Dog)	HARTZ 2 IN 1 PLUS LONG LASTING COLLAR FOR DOGS	Small	**900**	1,300	Product formulation amendments submitted on or about July 1, 2020
		Large	2,000	2,600	
2596-63 (Cat)	HARTZ 2 IN 1 PLUS LONG LASTING COLLAR FOR CATS	Small	**570**	**NA***	Voluntary cancellation submitted on July 10, 2020
		Large	1,300	**NA***	
2596-83 (Cat)	HARTZ 2 IN 1 PLUS SEVEN MONTH COLLAR FOR CATS	Small	**710**	**NA***	Product formulation amendments submitted on or about July 1, 2020 Amendments submitted on or
		Medium	**770**	1,500	
		Large	**910**	1,700	

					about July 1, 2020 to restrict use by animal weight, i.e., not for use on small cats (must weigh 5 pounds or more)
2596-84 (Dog)	HARTZ 2 IN 1 PLUS SEVEN MONTH COLLAR FOR DOGS	Small	**900**	1,300	Product formulation amendments submitted on or about July 1, 2020
		Large	2,000	2,600	
2596-139 (Cat)	HARTZ RABON COLLAR WITH METHOPRENE	Small	**850**	**NA***	Product formulation amendments submitted on or about July 1, 2020 Amendments submitted on or about July 1, 2020 to restrict use by animal weight, i.e., not for use on small cats (must weigh 5 pounds or more)
		Medium	1,400	1,500	
		Large	2,300	1,700	
2596-139 (Dog)		Small	**340**	1,300	Product formulation amendments submitted on or about July 1, 2020
		Medium	**790**	2,200	
		Large	1,200	2,600	

*N/A – this scenario is no longer applicable and MOEs are not presented due to the proposed label amendment to restrict use by animal weight (i.e., the products cannot be used on small cats) or because the product will be voluntarily cancelled (EPA Registration No. 2596-63).

VI. Conclusion

The July 2020 revised residential exposure and risk assessment supports EPA's responses to NRDC's Petition regarding whether TCVP pet uses pose unacceptable risks. EPA declines to revisit the 2006 RED or to perform a new cumulative risk assessment for organophosphates at this time, and notes that registration review of TCVP, along with the other organophosphates, is currently underway, pursuant to FIFRA § 3(g) and 40 CFR Part 155.

The July 2020 revised residential exposure and risk assessment discussed above uses appropriate, validated methodologies to calculate potential exposure to TCVP pet products and shows that all uses associated with TCVP liquid spray pet products result in no risks of concern. Remaining pet products containing TCVP will be voluntarily cancelled or uses terminated under FIFRA section 6(f), or registrations and labeling amended. As long as EPA can approve these requests, there will no longer be any risks of concern. Specifically, the registrants have agreed to either delete uses on cats and dogs from their dust products or voluntarily cancel their dust products; Hartz is cancelling registration for EPA Registration No. 2596-63, a cat collar; and the revised residential pet product risk assessment does not find risks of concern for the remaining pet collars containing TCVP, as those registrations are being amended. That is, for some TCVP products, voluntary cancellation has been initiated under section 6(f) of FIFRA, and the amendment process has been initiated to resolve risk concerns for all other TCVP pet products. Thus, cancellation of any TCVP pet product under section 6(b) of FIFRA is not necessary. In the unlikely event that EPA will not be able to grant amendments that remove the risks of concern, EPA will take appropriate regulatory action to address these registrations.

Therefore, based on the actions above, NRDC's Petition to cancel all pet uses for TCVP due to risks of concern is hereby DENIED.

VII. References

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Attachment A. Summary of TCVP Supplemental Distributor Pet Products.

Table A.1. Summary of TCVP Supplemental Distributor Pet Products.

Hartz EPA Reg. No.	Product name	Supplemental Distributor Name	Supplemental Distributor Number	Product names
2596-49 (Cat)	HARTZ 2 in 1 COLLAR FOR CATS	UPJOHN COMPANY	2596-49-9156	UNIPET FLEA & TICK COLLAR (FOR CATS)
		VMX PET PRODUCTS CORP	2596-49-62725	COLLAR FOR CATS
2596-50 (Dog)	HARTZ 2 in 1 COLLAR FOR DOGS	UPJOHN COMPANY	2596-50-9156	UNIPET FLEA & TICK COLLAR (FOR DOGS & PUPPIES)
		VMX PET PRODUCTS CORP	2596-50-62725	COLLAR FOR DOGS
2596-62 (Dog)	HARTZ 2 IN 1 PLUS LONG LASTING COLLAR FOR CATS	SOLVAY VETERINARY INC.	2596-62-734	SQUIBB TICK & FLEA COLLAR FOR DOGS
		TARGET CORPORATION	2596-62-13344	PHASE-OUT FLEA & TICK COLLAR FOR DOGS
		WAKEFERN FOOD CORP	2596-62-17704	SHOPRITE FLEA & TICK COLLAR FOR DOGS
		PETCO ANIMAL SUPPLIES INC.	2596-62-57286	PET GOLD BLUE FLEA & TICK COLLAR FOR DOGS
				PET GOLD WHITE FLEA & TICK COLLAR FOR PUPPIES
				PET GOLD WHITE FLEA & TICK COLLAR FOR DOGS
				PET GOLD WHITE FLEA & TICK COLLAR FOR LARGE DOGS
		VMX PET PRODUCTS CORP	2596-62-62725	FLEA & TICK COLLAR FOR DOGS
				RELEVE PET PROTECTION SYSTEM FLEA AND TICK COLLAR FOR DOGS BRIGHT BLUE
				RELEVE PET PROTECTION SYSTEM FLEA AND TICK COLLAR FOR DOGS BRIGHT RED
				RELEVE PET SYSTEM FLEA & TICK COLLAR FOR DOGS - BRIGHT BLUE
				RELEVE PET PROTECTION SYSTEM FLEA & TICK COLLAR FOR DOGS - BRIGHT RED

Table A.1. Summary of TCVP Supplemental Distributor Pet Products.				
Hartz EPA Reg. No.	Product name	Supplemental Distributor Name	Supplemental Distributor Number	Product names
		PACIFIC COAST DISTRIBUTING INC	2596-62-66578	TOP PAW FLEA & TICK ORANGE COLLAR DOGS
				TOP PAW FLEA & TICK BLUE COLLAR FOR DOGS
				TOP PAW FLEA & TICK WHITE COLLAR FOR DOGS
				TOP PAW FLEA & TICK WHITE COLLAR FOR PUPPIES
				TOP PAW FLEA & TICK RED COLLAR FOR DOGS
				DEFY 1-2-3 3 STEP PET PROTECTION SYSTEM FLEA & TICK COLLAR FOR PUPPIES
				DEFY 1-2-3 3 STEP PET PROTECTION SYSTEM FLEA & TICK COLLAR FOR DOGS
2596-63 (Cat)	HARTZ 2 IN 1 PLUS LONG LASTING COLLAR FOR CATS	SOLVAY VETERINARY INC.	2596-63-734	SQUIBB TICK & FLEA COLLAR FOR CATS
		WAKEFERN FOOD CORP	2596-63-17704	SHOPRITE FLEA & TICK COLLAR FOR CATS
		PETCO ANIMAL SUPPLIES INC.	2596-63-57286	PET GOLD WHITE FLEA & TICK COLLARS FOR CATS
				PET GOLD WHITE FLEA & TICK COLLAR FOR CATS
				PET GOLD WHITE FLEA & TICK COLLAR FOR KITTENS
				PET GOLD PURPLE FLEA & TICK COLLAR FOR CATS
		VMX PET PRODUCTS CORP	2596-63-62725	FLEA & TICK COLLAR FOR CATS
				RELEVE PET PROTECTION SYSTEM FLEA & TICK COLLAR FOR CATS - BRIGHT PURP
				RELEVE PET PROTECTION SYSTEM FLEA AND TICK COLLAR FOR CATS - BRIGHT PI
		PACIFIC COAST DISTRIBUTING INC	2596-63-66578	TOP PAW FLEA & TICK WHITE COLLAR FOR CATS
				TOP PAW FLEA & TICK WHITE COLLAR FOR KITTENS
				TOP PAW FLEA & TICK PURPLE COLLAR FOR CATS

Table A.1. Summary of TCVP Supplemental Distributor Pet Products.				
Hartz EPA Reg. No.	Product name	Supplemental Distributor Name	Supplemental Distributor Number	Product names
				DEFY 1-2-3 3 STEP PET PROTECTION SYSTEM FLEA & TICK COLLAR FOR CATS
				DEFY 1-2-3 3 STEP PET PROTECTION SYSTEM FLEA & TICK COLLAR FOR KITTENS
2596-83 (Cat)	HARTZ 2 IN 1 PLUS SEVEN MONTH COLLAR FOR CATS	VMX PET PRODUCTS CORP	2596-83-62725	RELEVE PET PROTECTION SYSTEM FLEA & TICK COLLAR FOR KITTENS
				RELEVE PET PROTECTION SYSTEM 7 MONTH FLEA & TICK COLLAR FOR CATS - BRI
				RELEVE PET PROTECTION SYSTEM 7 MONTH FLEA AND TICK COLLAR FOR CATS -
				RELEVE PET PROTECTION SYSTEM 7 MONTH FLEA AND TICK COLLAR FOR CATS - B
		CENTRAL GARDEN & PET COMPANY	2596-83-89459	ZODIAC BREADWAY FLEA & TICK COLLAR FOR CATS
2596-84 (Dog)	HARTZ RABON COLLAR WITH METHOPRENE	VMX PET PRODUCTS CORP	2596-84-62725	RELEVE PET PROTECTION SYSTEM 7 MONTH FLEA AND TICK COLLAR FOR DOGS - B
				RELEVE PET PROTECTION SYSTEM FLEA & TICK COLLAR FOR PUPPIES
				RELEVE PET PROTECTION SYSTEM 7 MONTH FLEA & TICK COLLAR FOR DOGS - BRI
				RELEVE PET PROTECTION SYSTEM 7 MONTH FLEA & TICK COLLAR FOR DOGS - BRI
				RELEVE PET PROTECTION SYSTEM 7 MONTH FLEA & TICK COLLAR FOR DOGS - BRI
		CENTRAL GARDEN & PET COMPANY	2596-84-89459	ADAMS FLEA & TICK COLLAR FOR DOGS
				ZODIAC FLEA & TICK COLLAR FOR DOGS
2596-139 (Cat & Dog)	HARTZ RABON COLLAR WITH METHOPRENE	FARNAM COMPANIES, INC.	2596-139-270	ADAMS FLEA & TICK CONTROL COLLAR FOR SMALL DOGS

Table A.1. Summary of TCVP Supplemental Distributor Pet Products.				
Hartz EPA Reg. No.	Product name	Supplemental Distributor Name	Supplemental Distributor Number	Product names
				ADAMS FLEA & TICK CONTROL COLLAR FOR LARGE DOGS
		WELLMARK INTERNATIONAL	2596-139-2724	VET.KEM OVITROL PLUS COMPLETE FLEA COLLAR WITH PRECOR INSECT GROWTH RE
				ZODIAC FLEATROL THE DUAL ACTION FLEA CONTROL COLLAR FOR DOGS & PUPPIES
				ZODIAC FLEATROL THE DUAL ACTION FLEA CONTROL COLLAR FOR CATS & KITTENS
				PREFLEA CONTINUOUS ACTION FLEA CONTROL COLLAR FOR DOGS & PUPPIES
				PREFLEA CONTINUOUS ACTION FLEA CONTROL COLLAR FOR CATS & KITTENS
				PREFLEA CONTINUOUS ACTION FLEA COLLAR FOR CATS & KITTENS 2596-139
				PREFLEA CONTINUOUS ACTION FLEA COLLAR FOR DOGS & PUPPIES
				ZODIAC POWER BAND FLEA & TICK COLLAR FOR CATS
				ZODIAC VETERINARIAN QUALITY FLEATROL POWERBAND FLEA & TICK COLLAR FOR
				ZODIAC FLEATROL POWERBAND FLEA & TICK COLLAR FOR CATS & KITTENS
				ZODIAC VETERINARIAN QUALITY FLEATROL POWERBAND FLEA & TICK COLLAR

Table A.1. Summary of TCVP Supplemental Distributor Pet Products.				
Hartz EPA Reg. No.	Product name	Supplemental Distributor Name	Supplemental Distributor Number	Product names
		INTERVET INC	2596-139-54382	OVITROL PLUS COMPLETE FLEA COLLAR FOR CATS AND KITTENS
		VMX PET PRODUCTS CORP	2596-139-62725	RELEVE PET PROTECTION SYSTEM FLEA & FLEA EGG KILLING COLLAR FOR CATS
				RELEVE PET PROTECTION SYSTEM FLEA & FLEA EGG KILLING COLLAR FOR DOGS
				RELEVE PET PROTECTION SYSTEM 7 MONTH FLEA & FLEA EGG COLLAR FOR PUPPIES
				RELEVE PET PROTECTION SYSTEM 7 MONTH FLEA & FLEA EGG COLLAR WITH SAFET
		CENTRAL GARDEN & PET COMPANY	2596-139-89459	BIO SPOT ACTIVE CARE COLLAR FOR DOGS AND PUPPIES
				ADAMS FLEA & TICK CONTROL COLLAR FOR DOGS
				ADAMS FLEA TICK CONTROL COLLAR FOR CATS

Attachment B. Tetrachlorvinphos: Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: July 20, 2020

SUBJECT: Tetrachlorvinphos: Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses.

PC Code: 083701, 083702
Decision No.: 559447
Petition No.: N/A
Risk Assessment Type: Residential Exposure Assessment
TXR No.: NA
MRID No.: NA

DP Barcode: D457031
Registration Nos.: NA
Regulatory Action: Registration Review
Case No.: 1321

CAS No.: 961-11-5, 22248-79-9
40 CFR: NA

FROM: Kelly Lowe, Environmental Scientist
Risk Assessment Branch V/VII (RAB V/VII)
Health Effects Division (HED; 7509P)
Office of Pesticide Programs

THROUGH: Michael Metzger, Chief
RABV and RABVII/HED (7509P)

And

Wade Britton, MPH, Environmental Health Scientist
Risk Assessment Branch IV (RABIV)

TO: Patricia Biggio, Chemical Review Manager
Dana Friedman, Branch Chief
Risk Management and Implementation Branch I (RMIBI)
Pesticide Re-evaluation Division (PRD; 7508P)
Office of Pesticide Programs

Introduction

The Health Effects Division (HED) conducted an updated non-occupational residential exposure and risk assessment for all TCVP pet uses. While this updated pet-product risk assessment only addresses the currently registered TCVP pet uses, the registration review risk assessment currently underway addresses all uses of TCVP. This document only presents HED's assessment of potential non-dietary exposures from the use of TCVP pet products (not dietary exposure).

In 2016, a final occupational and residential exposure (ORE) assessment of TCVP exposures[1] was conducted. Since then, additional data addressing the registered pet collar uses of TCVP have been submitted to the Agency and reviewed. The following updates have been included in this current assessment:

- The residential post-application exposure assessment for pet collars has been updated to reflect updated application rates for certain pet collars, incorporation of additional pet collar specific TCVP transferable residue and formulation type (i.e., liquid/solid) data that were submitted since the last ORE assessment, and inclusion of an adjustment factor for trimming of pet collars when applied to animals (i.e., 20% removal after application).

It is HED policy to use the best available data to assess exposure. Several sources of generic data were used in this assessment as surrogate data in the absence of chemical-specific data, including the Residential SOPs (Treated Pets). In addition, a TCVP dust/powder applicator exposure study (MRID 45519601) and a TCVP dust and pump spray study (MRID 45485501) were also used. Some of these data are proprietary, and subject to the data protection provisions of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

Data were also used from a literature study using TCVP pet collars, *Davis, M. et. al., Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos. Journal of Exposure Science and Environmental Epidemiology. (2008) 18, 564-57).* This study, herein referred to as the "Davis study," underwent review by the Human Studies Review Board (HSRB) on January 12 -13, 2016.

Note: This memorandum was originally reviewed by the Exposure Science Advisory Committee (ExpoSAC) on December 1, 2016.

[1] W. Britton et al. Tetrachlorvinphos: Final Occupational and Residential Exposure Assessment for Registration Review. 12/21/2016. D436833.

Table of Contents

1.0 Executive Summary

TCVP [(Z)-2-chloro-1-(2,4,5-trichlorophenyl) vinyl dimethyl phosphate] (also referred to as tetrachlorovinphos) is a member of the organophosphate (OP) class of pesticides. TCVP is used as a direct animal treatment to livestock (i.e., cattle, horses, poultry and swine) and their premises, in kennels, outdoors as a perimeter treatment, and as a flea treatment on cats and dogs.

In 2016, a final occupational and residential (ORE) assessment of TCVP exposures was conducted[2]. Since then, additional data addressing the registered pet collar uses of TCVP have been submitted to the Agency and reviewed. The following updates have been included in this current assessment:

- The residential post-application exposure assessment for pet collars has been updated to reflect updated application rates for certain pet collars, incorporation of additional pet collar specific TCVP transferable residue (MRID 50881801[3]) and formulation type data (i.e., dust torsion study, MRID 50931601[4]) that were submitted since the last ORE assessment, and inclusion of an adjustment factor for trimming of pet collars when applied to animals (i.e., 20% removal after application).

Exposure and Use Profile

The TCVP pet use formulations include collars, dusts/powders, and liquid (pump and trigger) sprays. Residential handler and post-application exposures are anticipated from the use of TCVP pet products. Residential TCVP handler exposures are anticipated to be short-term (1 to 30 days) and post-application exposures are anticipated to be short- (1 to 30 days), intermediate-term (1 to 6 months), and long-term (>6 months – *for pet collar scenarios only*) in duration.

Hazard

For TCVP, like other OPs, the initiating event in the adverse outcome pathway/mode of action (AOP/MOA) involves inhibition of the enzyme acetylcholinesterase (AChE) *via* phosphorylation of the serine residue at the active site of the enzyme. This inhibition leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system. TCVP does not require metabolic activation to an oxon to inhibit AChE; i.e., the parent compound is the active form inhibiting AChE. OPs generally exhibit a phenomenon known as steady state AChE inhibition. After repeated dosing at the same dose, the degree of inhibition comes into equilibrium with the production of new, uninhibited enzyme. At this point, the amount of AChE inhibition at a given dose remains consistent across duration. In general, OPs reach steady state within 2-3 weeks; a pattern that is observed for most OPs, but not every OP, like TCVP, which shows no difference in response across duration. For TCVP the steady state is reached after a single day of exposure. As such, the endpoint selection for TCVP considers data available for all durations of dosing when choosing the most protective point of departure.

[2] W. Britton et al. Tetrachlorvinphos: Final Occupational and Residential Exposure Assessment for Registration Review. 12/21/2016. D436833.
[3] MRID 50881801. D453149, K. Lowe et al., 12/05/2019. TCVP: Review and Summary of Residue Transfer Studies Submitted.
[4] MRID 50931601. D454190, K. Lowe et al., 12/03/2019. Submitted in response to GDCI-083702-1791.

No quantification of dermal non-cancer risk is required for TCVP since there were: (1) no treatment related effects (no clinical signs) at doses up to and including the limit dose of 1000 mg/kg/day in the dermal toxicity study; (2) both red blood cell (RBC) and brain cholinesterase activity were assessed in the dermal study and neither compartment was affected at the limit dose; (3) no quantitative susceptibility was observed for juvenile or gestational lifestages in the developmental, reproductive, or comparative cholinesterase study (CCA) toxicity studies. High quality AChE data for the other routes are available and allow for route specific evaluation. RBC AChE inhibition was observed in both sexes in the inhalation study (brain AChE was not assessed).

TCVP is classified as a Group C possible human carcinogen (based on statistically significant increases in combined hepatocellular adenoma/carcinoma in female mice) with a linear low-dose approach for quantification of risk using the oral slope factor (Q1*) of 1.83×10^{-3} $(mg/kg/day)^{-1}$. Whereas parent compound TCVP is the residue of concern for AChE inhibition, TCVP plus metabolites containing the 2,4,5 trichlorobenzene moiety are the residues of concern for cancer assessment. For purposes of calculating dermal doses for cancer assessment, a dermal absorption factor of 9.6% was used based on a dermal penetration study in rats.

Uncertainty Factors

For TCVP, as for other OPs, a database uncertainty factor (UF_{DB}) of 10X has been included for all residential exposure scenarios since the science addressing neurodevelopmental effects related to the OPs remains unresolved.

For the residential incidental oral exposures, the level of concern (LOC) is 1000 (i.e., risk estimates are not of concern when the MOE is $\geq$ the LOC) which includes a 10X uncertainty factor for interspecies extrapolation, a 10X uncertainty factor for intraspecies variation, and a 10X additional UF_{DB}. For the residential inhalation exposures, the LOC is 300 which includes a 3X uncertainty factor for interspecies extrapolation, a 10X uncertainty factor for intraspecies variation, and a 10X additional UF_{DB}. The interspecies extrapolation factor for the inhalation route has been reduced from 10X to 3X because the reference concentration (RfC) methodology for inhalation has been used to determine a human equivalent concentration (HEC) and takes into consideration the pharmacokinetic differences between animals and humans.

Residential Exposure and Risk

Residential Handler

There is the potential for residential handler dermal and inhalation exposures. Residential handler non-cancer dermal risks for all TCVP pet products have not been quantitatively assessed due to the finding of no dermal hazard for TCVP. Dermal doses have been calculated for estimation of cancer risks for adults only.

Pet Collars: The residential handler assessment for the TCVP pet collars was performed assuming pet collars are a combination of liquid and dust formulations, assuming a 99.62% liquid/0.38% dust ratio based on a TCVP chemical-specific dust torsion study[5]. Inhalation margins of exposure (MOEs) range from 240,000 to 1,200,000 and are not of concern (i.e.,

[5] MRID 50931601. D454190, K. Lowe et al., 12/03/2019. Submitted in response to GDCI-083702-1791.

MOEs ≥ the LOC of 300). Residential handler estimated cancer risks (combined dermal and inhalation) for TCVP pet collars assuming a 99.62% liquid/0.38% dust formulation ratio are all 10^{-8}.

Dust/Powder and Liquid Spray: No non-cancer inhalation risk estimates of concern were identified for residential handlers for the TCVP pet dust/powder and liquid spray formulations. Inhalation MOEs for both formulations range from 5,600 to 160,000 and are not of concern (i.e., MOEs ≥ the LOC of 300). Residential handler estimated cancer risks (combined dermal and inhalation) for TCVP dusts/powders range from 10^{-9} to 10^{-7}, and for liquid sprays range from 10^{-9} to 10^{-8}.

Residential Post-application

There is the potential for both dermal and incidental oral (hand-to-mouth) post-application exposures from the pet uses of TCVP. Post-application inhalation exposure to treated pets is assumed to be negligible and has not been quantitatively assessed. Since there is no non-cancer dermal hazard for TCVP, non-cancer dermal post-application risks were not quantified for adults and children.

Pet Collars: The incidental oral post-application assessment for the TCVP pet collars was performed assuming pet collars are a combination of liquid and dust formulations, assuming a 99.62% liquid/0.38% dust ratio based on the available TCVP chemical-specific torsion study mentioned above. The application rate for pet collars has been adjusted to account for trimming of the pet collar when applied to an animal. The adjustment factor is based on information provided in a TCVP efficacy study submitted for dog collars[6]. In addition, HED has presented post-application risks using two available transferable residue studies: a literature study (i.e., the Davis study[7]) and a TCVP pet collar residue transfer study (MRID 50881801[8]). Both studies have been deemed acceptable for risk assessment and indicate similar fraction transfer values. Therefore, both studies have been included in the non-cancer assessment and residential post-application risks have been presented using both sets of data. For the calculation of potential cancer risk estimates, a fraction transferred value from the Davis study (which allowed for calculation of potential transfer over a longer duration, 112 days) was used.

Assuming a 99.62% liquid/0.38% dust formulation ratio, the residential steady-state non-cancer incidental oral MOEs for children (1 to <2 years old) exposed to pets treated with TCVP pet collars ranged from 340 to 2,300 and are of concern (i.e., not all MOEs ≥ the LOC of 1000). Assuming a 99.62% liquid/0.38% dust formulation ratio, residential post-application cancer (adult only) risk estimates for TCVP pet collars range from 10^{-7} to 10^{-6}.

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[6] MRID 51079501. *Efficacy and Repellence of Ectoparsiticidal Treatments Against Ticks (Dermacentor Variabilis, Ixodes Scapularis, Rhipicephaslus Sanguineus), Fleas (Ctenocephalides Felis) and Mosquitos (Aedes Aegypti) on Dogs*. May 7, 2019. Table 4 (p. 37 – 39).

[7] D430707, W. Britton, 12/16/2015. Davis, M. et. al., *Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos*. Journal of Exposure Science and Environmental Epidemiology. (2008) 18, 564-57).

[8] MRID 50881801. D453149, K. Lowe et al., 12/05/2019. TCVP: Review and Summary of Residue Transfer Studies Submitted.

Dust/Powder and Liquid Spray: Residential non-cancer incidental oral MOEs for children (1 to < 2 years old) exposed to pets treated with TCVP dust/powders range from 98 to 640 and are of concern (i.e., MOEs < the LOC of 1000). Residential non-cancer incidental oral MOEs for children (1 to < 2 years old) exposed to pets treated with TCVP liquid spray products range from 1,600 to 15,000 and are not of concern (i.e., MOEs ≥ the LOC of 1000). Residential post-application cancer (adult only) risks estimated for TCVP dust/powder products range from 10^{-7} to 10^{-6}, and for TCVP liquid sprays are all 10^{-7}.

Human Studies Review

This risk assessment relies in part on data from studies in which human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies used to develop the Residential SOPs (Treated Pets); as well as registrant-submitted studies including a TCVP dust/powder applicator exposure study (MRID 45519601) and a TCVP dust and pump spray study (MRID 45485501) are (1) subject to ethics review pursuant to 40 CFR 26, (2) have received the review necessary for consideration in this assessment, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have included review by the Human Studies Review Board (HSRB). Descriptions of data sources, as well as guidance on their use, can be found at the Agency website[9].

Data were also used from a literature study using TCVP pet collars, *Davis, M. et. al., Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos. Journal of Exposure Science and Environmental Epidemiology. (2008) 18, 564-57).* On January 12-13, the EPA HSRB met to address the scientific and ethical charge questions related to Davis study. The HSRB concluded that, "the research is scientifically sound and, if used appropriately, the pet fur transferable residue data from the rubbing protocol used in the study can provide useful information for evaluating potential exposures of adults and children from contact with dogs treated with tetrachlorvinphos containing pet collars."[10]

2.0 Risk Assessment Conclusions and Recommendations

2.1 Summary of Risk Estimates

Residential Handler

Pet Collars: No non-cancer steady-state inhalation risk estimates of concern were identified for residential handlers for pet collars assuming a 99.62% liquid/0.38% dust formulation ratio. Inhalation MOEs range from 240,000 to 1,200,000 and are not of concern (i.e., MOEs ≥ the LOC of 300). Residential handler cancer risks estimated for TCVP pet collars assuming a 99.62% liquid/0.38% dust formulation ratio are all 10^{-8}.

[9] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data and https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-post-application-exposure

[10] Letter from Liza Dawson, PhD, Chair of the EPA HSRB to Thomas Burke, PhD, MPH, EPA Science Advisor. Subject: January 12-13, 2016 EPA Human Studies Review Board Meeting Report. March 30, 2016.

Dust/Powder and Liquid Spray: No non-cancer inhalation risk estimates of concern were identified for residential handlers for the TCVP pet dust/powder and liquid spray formulations. Inhalation MOEs for both formulations range from 5,600 to 160,000 and are not of concern (i.e., MOEs ≥ the LOC of 300). Residential handler estimated cancer risks (combined dermal and inhalation) for TCVP dusts/powders range from 10^{-9} to 10^{-7}, and for liquid sprays range from 10^{-9} to 10^{-8}.

Residential Post-application

Pet Collars: Assuming a 99.62% liquid/0.38% dust formulation ratio, the residential steady-state non-cancer incidental oral MOEs for children (1 to <2 years old) exposed to pets treated with TCVP pet collars ranged from 340 to 2,300 and are of concern (i.e., not all MOEs ≥ the LOC of 1000). Assuming a 99.62% liquid/0.38% dust formulation ratio, residential post-application cancer (adult only) risk estimates for TCVP pet collars range from 10^{-7} to 10^{-6}.

Dust/Powder and Liquid Spray: Residential non-cancer incidental oral MOEs for children (1 to < 2 years old) exposed to pets treated with TCVP dust/powders are of concern and range from 98 to 640 (i.e., MOEs < the LOC of 1000). Residential non-cancer incidental oral MOEs for children (1 to < 2 years old) exposed to pets treated with TCVP liquid spray products are not of concern and range from 1,600 to 15,000 (i.e., MOEs are ≥ the LOC of 1000). Residential post-application cancer (adult only) risks estimated for TCVP dust/powder products range from 10^{-7} to 10^{-6}, and for TCVP liquid sprays are all 10^{-7}.

3.0 Hazard Characterization and Dose-Response Assessment

TCVP is a member of the OP class of pesticides. For TCVP, like other OPs, the initiating event in the adverse outcome pathway/mode of action (AOP/MOA) involves inhibition of the enzyme acetylcholinesterase (AChE) *via* phosphorylation of the serine residue at the active site of the enzyme. This inhibition leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system. TCVP does not require metabolic activation to an oxon to inhibit AChE; i.e., the parent compound is the active form inhibiting AChE. OPs generally exhibit a phenomenon known as steady state AChE inhibition. After repeated dosing at the same dose, the degree of inhibition comes into equilibrium with the production of new, uninhibited enzyme. At this point, the amount of AChE inhibition at a given dose remains consistent across duration. In general, OPs reach steady state within 2-3 weeks; a pattern that is observed for most OPs, but not every OP, like TCVP, which shows no difference in response across duration. For TCVP the steady state is reached after a single day of exposure. As such, the endpoint selection for TCVP considers data available for all durations of dosing when choosing the most protective point of departure.

Acute Toxicity

In acute lethality studies, TCVP has low acute toxicity by the oral, dermal, and inhalation routes of exposure. It is a slight dermal irritant, a moderate eye irritant, and a dermal sensitizer.

Table A.3.1 Acute Toxicity Profile – Tetrachlorvinphos Technical				
Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute Oral (rat)	41222504	LD_{50} = 1480 mg/kg (M & F) LD_{50} > 469 and < 965 mg/kg (F) LD_{50} = 995 mg/kg (C)	III
870.1200	Acute Dermal (rabbit)	41222505	LD_{50} > 20000 mg/kg (M & F)	III
870.1300	Acute Inhalation (rat)	00138933	LC_{50} > 3.61 mg/L (M & F)	IV*
870.2400	Primary Eye Irritation (rabbit)	41222506	Moderately irritating	III
870.2500	Primary Skin Irritation (rabbit)	41000507	Slightly irritating	IV
870.2600	Dermal Sensitization (guinea pig)	41377902 (99.0% a.i.)	Sensitizer (Buehler Method)	N/A
		42981011 (97.0% a.i.)	Sensitizer (Buehler Method)	N/A
870.6100	Acute Delayed Neurotoxicity	41905901	No clinical signs of neurotoxicity observed (NTE not measured)	N/A

* In the original review of this study, TXR 0007181, Y. Ioannou, 09/02/1987, the assigned Toxicity Category was III. Based on the current Acute toxicity Classification (Label Review Manual, 03/2018) the Toxicity Category would be IV.

Toxicological Points of Departure (PODs) Used for Risk Assessment

Incidental Oral, Steady State: The steady state incidental oral POD (2.8 mg/kg/day) was selected from an acute dose CCA study (MRID 448773401) in juvenile rats. A benchmark dose lower limit for 10% response ($BMDL_{10}$ or the lower confidence bound on the BMD_{10} which is the estimated dose where ChE is inhibited by 10% compared to background) of 2.8 mg/kg/day associated with RBC cholinesterase inhibition in male and female post-natal day (PND) 11 and 21 rats was selected as a suitable POD for the steady state incidental oral exposure scenario. The duration of this study is considered appropriate for this exposure scenario since AChE data across the TCVP database demonstrate that there is no progression of AChE inhibition over exposure duration, and steady state inhibition occurs essentially after a single dose.

Inhalation, Steady State: The steady state inhalation POD was selected from a 4-week inhalation toxicity study (MRID 48803501) in rats, based on an increase in RBC cholinesterase inhibition in both sexes. Males had slightly lower modeled values ($BMDL_{10}$ of 0.022 mg/L; BMD_{10} of 0.12 mg/L). The duration of this study is considered appropriate for the steady state exposure scenario. The methods and dosimetry equations described in the Agency's reference concentration (RfC) guidance are suitable for calculating human equivalent concentrations (HECs) based on the inhalation toxicity POD obtained in rats exposed for 6 hr/day for an average of 5.5 days/week. The regional deposited dose ratio (RDDR), which accounts for the particulate diameter (mass median aerodynamic diameter [MMAD] and geometric standard deviation [GSD] of aerosols) can be used to estimate the different dose fractions deposited along the respiratory tract surface areas. Thus, the RDDR can be used to adjust an observed inhalation particulate exposure of an animal to the predicted inhalation exposure for a human. For the subchronic inhalation toxicity study with TCVP, an RDDR of 2.525 was estimated based on extrarespiratory effects (RBC cholinesterase inhibition) in Sprague Dawley rats (bodyweight = 267g). The MMAD and GSD of 2.57 and 3.785 µm, respectively, at 0.05 mg/L were used to derive the RDDR.

The HECs are summarized in Table 3.2, as well as human equivalent doses (HEDs) calculated for residential and occupational handler scenarios. The standard interspecies extrapolation uncertainty factor can be reduced from 10X to 3X due to the HEC calculation accounting for pharmacokinetic (not pharmacodynamic) interspecies differences. The intraspecies uncertainty factor remains at 10X.

Table 3.2. Summary of HEC/HED Values for TCVP.

Population	Scenario	Tox Duration Adjustment		HEC[a]		HED[b]
		Hours/Day	Days/Week	mg/L	mg/m^3	mg/kg/day
Occupational	Handler	0.75	1	0.042	41.663	3.94
Residential	Handler	N/A	N/A	0.056	55.550	1.31
	Bystander	0.25	0.714	0.010	9.920	N/A

a. HEC = human-equivalent concentration; HED = human-equivalent dose.
Occupational Handler HEC = rat POD (0.022 mg/L) × daily duration adjustment (6/8 or 0.75) × weekly daily duration adjustment (5/5 or 1) × RDDR (2.525).
Residential Handler HEC = rat POD (0.022 mg/L) × RDDR (2.525).
Residential Bystander HEC = rat POD (0.022 mg/L) × daily duration adjustment (6/24 or 0.25) × weekly daily duration adjustment (5/7 or 0.714) × RDDR (2.525).

b. HED = HEC × human-specific conversion factor (11.8 L/hr-kg BW) × daily duration (8 hr for occupational and 2 hr for residential).

Dermal, Steady State: No quantification of dermal non-cancer risk is required for TCVP since there were: (1) no treatment related effects (no clinical signs) at doses up to and including the limit dose of 1000 mg/kg/day in the dermal toxicity study; (2) both RBC and brain cholinesterase activity were assessed in the dermal study and neither compartment was affected at the limit dose; and (3) no quantitative susceptibility was observed for juvenile or gestational lifestages in the developmental, reproductive, or CCA toxicity studies.

Cancer Classification: TCVP is classified as a Group C, possible human carcinogen, based on statistically significant increases in combined hepatocellular adenoma/carcinoma (primarily carcinomas) in the female B6C3F1 mouse, suggestive evidence of thyroid c-cell adenomas, and adrenal pheochromocytomas in the rat, as well as mutagenicity concerns. Following a reassessment of the mutagenicity data available on TCVP, it was determined that the relevance of the mutagenic findings to the tumorigenic response seen in female mice cannot be established. Therefore, a follow-up mouse micronucleus assay (OPPTS Harmonized Guideline 870.5395) is required for TCVP. Additionally, a study that investigates possible genotoxic activity in the target organ (liver) is required. This study should examine DNA damage potential (Comet assay, DNA adduct formation, or any other DNA target)[11]. A cancer potency factor (Q1 *) of 1.83×10^{-3} $(mg/kg/day)^{-1}$ was estimated using the Weibull 83 time-to-tumor model. A 3/4 body weight scaling factor was used to convert from mouse to human equivalents. Following the submission and review of the required assays, the need for an updated cancer assessment will be determined.

Uncertainty Factors

A LOC of 1000 (i.e., risk estimates are not of concern when the MOE is ≥ the LOC) is appropriate for the assessment of the oral route of exposures [10X for interspecies extrapolation,

[11] S. Dobreniecki, 5/01/2020, Tetrachlorovinphos (TCVP): Revisit of Mutagenicity Studies, TXR 0057553, D437226.

10X for intraspecies variation and a 10X UF_{DB}]. The UF_{DB} has been included due to uncertainty in the human dose-response relationship for neurodevelopmental effects[12]. For the inhalation route of exposure, a LOC of 300 is appropriate [3X for interspecies extrapolation, 10X for intraspecies variation, and 10X UF_{DB}]. The interspecies extrapolation is reduced from 10X to 3X because the reference concentration (RfC) methodology for inhalation is used to determine an HEC and takes into consideration the pharmacokinetic differences between animals and humans.

Absorption

Despite the determination of the lack of dermal hazard for TCVP, dermal exposures from TCVP must be quantified for the purpose of cancer risk assessment. Because the cancer assessment is based on an oral study, a dermal absorption factor (DAF) of 9.6% was used in the route-to-route extrapolation. This DAF is based on the results of a registrant submitted TCVP dermal penetration study in rats. Since the inhalation POD was based on a route-specific toxicity study, no absorption factor was necessary to estimate exposure.

Body Weight

For adults, when an endpoint is not sex-specific (i.e., the endpoints are not based on developmental or fetal effects), a body weight of 80 kg is typically used in risk assessment; however, in this case, a female-specific body weight of 69 kg was used. While the endpoint of concern, RBC AChE inhibition, is not sex-specific, the female body weight was used for pregnant women due to uncertainty in the human dose-response relationship for potential neurodevelopmental effects. A body weight of 11 kg was assumed for children 1 to < 2 years old.

Table 3.3. Summary of Toxicological Doses and Endpoints for TCVP for Use in Dietary and Non-Occupational Human Health Risk Assessments.

Exposure/ Scenario	Point of Departure	Uncertainty Factors*	Level of Concern	Study and Toxicological Effects
Incidental Oral (steady state)	$BMDL_{10}$ = 2.8 mg/kg/day	UF_A= 10X UF_H=10X UF_{DB} = 10X	Residential LOC for MOE = 1000	Repeat dose CCA study (MRID 48773401a) - Rat BMD_{10} = 3.2 mg/kg/day, based on PND 21 male RBC ChE inhibition
Dermal (steady state)	No potential hazard *via* the dermal route, based on the lack of treatment-related effects, including the lack of RBC and brain cholinesterase inhibition following repeat dermal exposure of rats at dose levels up to 1000 mg/kg/day and quantitative susceptibility was not observed.			
Inhalation (steady state)	$BMDL_{10}$=0.022 mg/L (males)	UF_A= 3X UF_H=10X UF_{DB} = 10X	Residential LOC for MOE = 300	Subchronic Inhalation Toxicity Study (MRID 48803501) – Rat

[12] For more information, please reference Sections 4.4 and 4.5 of the Tetrachlorvinphos (TCVP) Revised Human Health Risk Assessment for Registration Review. D. Drew *et al.* D436834. 12/21/2016.

Table 3.3. Summary of Toxicological Doses and Endpoints for TCVP for Use in Dietary and Non-Occupational Human Health Risk Assessments.				
Exposure/ Scenario	Point of Departure	Uncertainty Factors*	Level of Concern	Study and Toxicological Effects
				BMD_{10} = 0.12 mg/L, based on RBC ChE inhibition in both sexes
Cancer (oral, dermal, inhalation)	Classification: A possible human (Group C) carcinogen. Q_1^* = 1.83 x 10^{-3} $(mg/kg/day)^{-1}$			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies); MOE = margin of exposure. LOC = level of concern. RBC = red blood cell. $BMDL_{10}$= benchmark dose lower limit for 10% response.

*The 10X UF_{DB} is due to uncertainty in the human dose-response relationship for neurodevelopmental effects.

4.0 Use Profile

TCVP is used as a direct animal treatment to livestock (i.e., cattle, horses, poultry and swine) and their premises, in kennels, outdoors as a perimeter treatment, and as a flea treatment on cats and dogs. The TCVP pet product uses are formulated as follows: dusts, liquid (trigger/pump) sprays, and pet collars. This assessment only addresses the pet uses. A summary of all registered pet product TCVP labels and use directions are presented in Appendix A of this document.

5.0 Residential Exposure and Risk Estimates

Residential exposures (handler and post-application) are anticipated from the use of TCVP pet products for dogs and cats including collars, dusts/powders, and liquid sprays. Exposures are expected for adults who apply TCVP products to their pets and for adults and children who may contact previously treated pets.

Residential TCVP handler exposures are anticipated to be short-term (1 to 30 days) and post-application exposures are anticipated to be short- (1 to 30 days), intermediate- (1 to 6 months), and long-term (>6 months – *for pet collar scenarios only*). However, because of the steady state AChE inhibition exhibited by the OPs, steady state exposures were assessed and presented for residential exposures to TCVP pet products.

A risk assessment of all currently registered TCVP pet products was first completed in 2014 (D420283[13]). In 2015, these risk outcomes were updated during the ongoing Registration Review process (D426984[14]) to reflect the following changes: (1) the incidental oral and inhalation LOCs increased 10 fold due to uncertainty in the human dose-response relationship for potential neurodevelopmental effects, (2) the determination of no dermal hazard from TCVP,

[13] W. Britton. Residential Exposure Assessment in Response to the Natural Resources Defense Council Petition to Cancel All Pet Uses for Tetrachlorvinphos. 11/05/2014. D420283.

[14] W. Britton. Tetrachlorvinphos: Occupational and Residential Exposure Assessment for Registration Review. 12/21/2015. D426984.

and (3) the use of a female-specific body weight, 69 kg, for assessment of adult exposures instead of the average adult body weight of 80 kg due to uncertainty for potential neurodevelopmental effects. In 2016, a revised ORE assessment[15] was conducted to incorporate additional changes including: (1) the reduction of the incidental oral POD from a $BMDL_{10}$ of 8.0 mg/kg/day to 2.8 mg/kg/day, (2) the use of the literature study, Davis, M. *et. al*, *Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos. Journal of Exposure Science and Environmental Epidemiology.* ((2008) 18, 564-57), for assessment of residential post-application risks from exposures to TCVP pet collars, and (3) an updated pet collar assessment assuming that the TCVP pet collar product exists as a liquid and solid form concurrently (with varying ratios of liquid to dust).

Since the 2016 assessment, additional residue transfer data, as well as formulation data, have been submitted for TCVP pet collars. These data have been incorporated into this revised assessment.

5.1 Residential Handler Exposures

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task. Residential handlers are assumed to complete all elements of an application without use of any protective equipment.

Residential handler exposures to TCVP pet products may occur via the dermal or inhalation routes while the product is placed on a cat or dog. Both steady state non-cancer and cancer residential handler exposure assessments were performed for adult homeowners applying TCVP pet collars, dusts/powders, and liquid spray products to cats and dogs. Since there is no non-cancer dermal hazard for TCVP, the steady state (non-cancer) handler assessment includes only inhalation exposures. For the cancer assessment, both dermal and inhalation exposures are assessed.

Residential Non-Cancer Handler Exposure Data and Assumptions

Application Rate: The application rates used in the assessment of pet products typically represent the maximum amount of active ingredient (ai) that could be applied by weight of the treated animal (small, medium, and large). However, this is only possible when the product is manufactured for use, or is labeled specifically, for different animal weight ranges. If this information is not provided, a number of assumptions are used which are described in HED's 2012 Residential SOPs (Treated Pets SOP).

The majority of pet collar formulations are registered as a single collar for use on all animal weight ranges. These have been assumed for use on different weight ranges as specified in the Residential SOPs which include:

- Cats – Small (up to 5 lbs), Medium (6 to 12 lbs), Large (13 lbs and up).

[15] W. Britton et al. Tetrachlorvinphos: Final Occupational and Residential Exposure Assessment for Registration Review. 12/21/2016. D436833.

- Dogs - Small (up to 20 pounds), Medium (21 to 50 lbs) and Large (51 lbs and up).

While the pet collar product labels recommend trimming of the pet collar after it is applied to the animal, since the handler would be exposed to the full length of the collar during application, trimming of the collar was not accounted for in the residential handler exposure calculations.

For TCVP dusts/powders, all products identify a specific amount to use per animal weight that allows for determination of the maximum application rate. For TCVP liquid sprays, all registered products recommend the user to apply a specific number of "strokes" per animal size. In order to determine the amount of ai applied per treatment as specified by number of strokes, HED requested additional information from the product registrant. Hartz Mountain Corporation provided information regarding the volume of product released per stroke for pump and trigger spray products; 0.19 and 0.93 grams, respectively. Only trigger spray products are registered for dogs; however, both pump and trigger spray products are registered for cats. Additionally, per request of HED, in March 2014, Hartz Mountain Corporation amended the master label of EPA Reg. No. 2596-140 to recommend a number of strokes per animal size. Previously, a number of strokes per cat/dog were not recommended.

Pet Collar Formulation Issue: Per EPA's 2012 Residential SOPs[16], pet collar products are categorized as a liquid formulation (i.e., using inputs and assumptions reflective of liquid formulations). However, in NRDC's Petition related to TCVP pet uses, the NRDC asserted that EPA incorrectly considered the TCVP pet collar formulation to be a liquid formulated product noting that a label for a TCVP pet collar product states that 'as the collar begins to work, a fine white powder will appear on the surface.' HED reviewed this information and agreed that exposure to the active ingredient as a dust/solid formulation could occur. Therefore, HED updated the assessment for pet collars assuming the active ingredient is present as both liquid and solid forms concurrently. Due to the uncertainty associated with pet collar formulation type, and without chemical-specific data, HED typically assumes a range of ratios to cover the range of potential exposures (e.g., 1/99, 50/50, and 99/1 liquid/dust). This approach was taken for TCVP in the 2016 ORE assessment. However, since that assessment, a TCVP-specific dust torsion study was submitted and reviewed (MRID 50931601[17]). This study was submitted to address the uncertainty surrounding the ratio of liquid/dust in the TCVP pet collars. In the study, the weight difference of collar pieces before and after the torsion tests (which involved mechanical torsion and stress by twisting and pulling the collar three times) was measured. This weight difference was assumed to represent the amount of TCVP lost from the collar in the form of dust. Based on the results of this study, it was determined that 0.38% mass (assumed to be dust) is lost from the collar due to torsional stress. Therefore, in the current exposure and risk calculations for TCVP pet collars, HED assumed a liquid/dust ratio of 99.62/0.38.

Unit Exposures (UE): Since there is no dermal POD for TCVP, only inhalation exposures were assessed for residential handlers.

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[16] http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

[17] MRID 50931601. D454190, K. Lowe et al., 12/03/2019. Submitted in response to GDCI-083702-1791.

Chemical-specific unit exposure data were provided in support of residential handler risk assessment for the dust/powder formulations only (MRID 45519601). The study, "*Determination of Dermal and Inhalation Exposures to Tetrachlorovinphos (TCVP) During the Application of an Insecticide Powder to a Dog*," was previously reviewed by the Agency[18] and determined to be acceptable. The study resulted in an average unit exposure for the inhalation route of exposure of 3.1 mg/lb ai.

In the absence of exposure data for residential handling of pet collars and liquid sprays, HED used surrogate unit exposure values to estimate handler exposures. Surrogate exposure data for a groomer trigger pump spray application to dogs from the 2012 Residential SOPs[19] was used to estimate handler exposures from TCVP liquid spray products. For pet collars, when assuming a solid formulation, HED used the best available data, a TCVP dust/powder applicator exposure study (MRID 45519601). When assuming the TCVP pet collars are a liquid formulation, the liquid-specific unit exposure (UE) values (i.e., surrogate data from a spot-on applicator study) from the 2012 Residential SOPs were considered; however, the liquid formulation spot-on surrogate UE data assumes negligible inhalation exposure. Therefore, only the dust-specific UE data were used to assess potential inhalation exposures from application of pet collars.

Area Treated or Amount Handled: Per the 2012 Treated Pet SOP, it is assumed that residential handlers of pet treatment products will treat 2 animals per application.

Residential Non-Cancer Handler Exposure and Risk Equations

The algorithms used to estimate non-cancer exposure and dose for residential handlers can be found in Appendix B and/or the 2012 Residential SOPs.

Summary of Residential Handler Non-Cancer Exposure and Risk Estimates

Pet Collars: No non-cancer steady-state inhalation risk estimates of concern were identified for residential handlers for pet collars assuming a 99.62% liquid/0.38% dust formulation ratio. Inhalation MOEs range from 240,000 to 1,200,000 and are not of concern (i.e., MOEs $\geq$ the LOC of 300). Residential handler non-cancer risk estimates for pet collars are presented in Appendix Table C.2.

Dust/Powder and Liquid Spray: No non-cancer inhalation risk estimates of concern were identified for residential handlers for the TCVP pet dust/powder and liquid spray formulations. Inhalation MOEs for both formulations range from 5,600 to 160,000 and are not of concern (i.e., MOEs $\geq$ the LOC of 300). Residential handler non-cancer risk estimates for dust/powder and liquid spray products are presented in Appendix Table C.3.

Residential Cancer Handler Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential cancer handler risk assessment.

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[18] S. Hanley. HED's Review of *Determination of Dermal and Inhalation Exposures to Tetrachlorvinphos (TCVP) During the Application of an Insecticide Powder to a Dog.* 1/09/2002. D278626.

[19] http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

Days per Year of Exposure: For the purpose of assessing residential handler cancer exposure/risk from TCVP pet product application, HED has assumed 4 days per year for collars and 6 days per year for dusts/powders and liquid sprays. The collar is based on a worst-case assumption of a single application every 3 months. Collar re-treatment intervals range from 3 to 7 months. HED assumed a bi-monthly retreatment interval for dusts/powders and liquid sprays.

Years per Lifetime of Exposure: It is assumed that residential handlers would be exposed for 50 years out of a 78 year lifespan. This factor is routinely used as a conservative estimate of the number of years an individual could continually use a single pesticide product.

Lifetime Expectancy: Life expectancy values are from the Exposure Factors Handbook 2011 Edition Table 18-1 (U.S. EPA, 2011[20]). The table shows that the overall life expectancy is 78 years based on life expectancy data from 2007. In 2007, the average life expectancy for males was 75 years and 80 years for females. Based on the available data, the recommended value for use in cancer risk assessments is 78 years.

Residential Handler Cancer Exposure and Risk Estimate Equations

Cancer risk estimates were calculated using a linear low-dose extrapolation approach in which a Lifetime Average Daily Dose (LADD) is first calculated and then compared with a Q_1* that has been calculated for TCVP based on dose response data in the appropriate toxicology study (Q_1* = 1.83 x 10^{-3} $(mg/kg/day)^{-1}$). Absorbed average daily dose (ADD) levels were used as the basis for calculating the LADD values. Dermal and inhalation ADD values were first added together to obtain combined ADD values. LADD values were then calculated and compared to the Q_1* to obtain cancer risk estimates.

The algorithms used to estimate the LADD and cancer risk for residential handlers can be found in Appendix B.

Summary of Residential Handler Cancer Exposure and Risk Estimates

Pet Collars: Residential handler cancer risks estimated for TCVP pet collars assuming a 99.62% liquid/0.38% dust formulation ratio are all 10^{-8}. Residential handler cancer risk estimates for pet collars are presented in Appendix Table D.1.

Dust/Powder and Liquid Sprays: Residential handler cancer risks for TCVP dusts/powders range from 10^{-9} to 10^{-7}, and for liquid sprays range from 10^{-9} to 10^{-8}. Residential handler cancer risk estimates for dust/powder and liquid spray products are presented in Appendix Table D.2.

5.2 Residential Post-application Exposure/Risk Estimates

There is the potential for post-application exposure for individuals exposed as a result of contacting a cat/dog previously treated with TCVP pet products (dusts/powders, liquid sprays, pet collars).

[20] https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252.

Since there is no non-cancer dermal hazard for TCVP, a quantitative non-cancer post-application dermal exposure assessment was not performed for adults or children. A quantitative residential post-application inhalation exposure assessment was not performed as inhalation exposure is expected to be negligible from applications to pets. The quantitative exposure/risk assessment for residential post-application exposures is based on the following scenario: Post-application incidental oral (hand-to-mouth) exposure (children 1 to < 2 years old only) from contacting cats and dogs treated with TCVP.

The lifestages selected for each post-application scenario (i.e., children 1 to < 2 years old) are based on an analysis provided as an Appendix in the 2012 Residential SOPs[21]. While not the only lifestage potentially exposed for these post-application scenarios, the lifestage that is included in the quantitative assessment is health protective for the exposures and risk estimates for any other potentially exposed lifestage.

Residential Non-Cancer Post-Application Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential non-cancer post-application risk assessment.

Application Rate: The application rates used in the assessment of pet products typically represent the maximum amount of active ingredient (ai) that could be applied by weight of the treated animal (small, medium, and large). However, this is only possible when the product is manufactured for use, or is labeled specifically, for different animal weight ranges. If this information is not provided, a number of assumptions are used which are described in HED's 2012 Residential SOPs (Treated Pets SOP).

For pet collars, the label typically directs users to cut off and dispose of any excess length once the product is fit and buckled into place. In the previous TCVP assessment, since data indicating the exact length that is cut off was not available, it was assumed that individuals would be exposed to the full length of the collar per the Treated Pet SOP. Since that time, the Registrant has submitted pet collar efficacy data to address this uncertainty. The data provided (from MRID 51079501[22]) is from a 7-month efficacy study in dogs. A total of 63 dogs (range in weights of 11 to 22 kg) were included in the data summary, and the weights of the collars were provided, including the pre-cut weight, the weight of the cut-off piece, and the weight of the fitted collar. The percent of collar removed was calculated by taking the weight of the cut-off piece and dividing by the weight of the pre-cut collar. The percent of the collar removed ranged from 20% to 43%, with an average of 30% being removed. In order to provide a conservative assumption of how much collar might be removed during use, HED has chosen to use a value of 20% to adjust the application rate for pet collars. Accounting for the percentage of the pet collar removed is believed to better represent typical usage of the product as it is fit to the treated animal.

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[21] Available: http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

[22] MRID 51079501. *Efficacy and Repellence of Ectoparsiticidal Treatments Against Ticks (Dermacentor Variabilis, Ixodes Scapularis, Rhipicephaslus Sanguineus), Fleas (Ctenocephalides Felis) and Mosquitos (Aedes Aegypti) on Dogs*. May 7, 2019. Table 4 (p. 37 – 39).

Pet Collar Formulation Type Approach: As was mentioned in Section 5.1, in the current exposure and risk calculations for TCVP pet collars, HED assumed a liquid/dust ratio of 99.62/0.38. For the residential post-application exposure assessment, the Agency used inputs and assumptions [e.g., transfer coefficients (dermal exposures) and the fraction of active ingredient on hands from the transfer coefficent studies (hand-to-mouth exposures)] specific to both liquid and solid formulation types when assessing pet collar exposures.

Transfer Data: Chemical-specific residue transfer studies were used for assessment of post-application exposures from registered TCVP pet products. For dust/powder products and liquid sprays, HED relied on a TCVP powder and pump spray study (MRID 45485501). In 2014, in support of the Agency's response to the NRDC Petition, the study was reevaluated based on current standards of conduct for pet residue transfer studies.[23] For the purposes of the non-cancer assessment, the transferable residue from the day of application (day 0) was used as follows: 0.048% (maximum observed) for dusts/powders and 0.81% for liquid sprays (maximum observed).

For pet collars, HED has used two TCVP-specific residue transfer studies available for pet collars. The first is a literature study[24] (the Davis study), which was used previously, and the second is a newly submitted TCVP pet collar residue transfer study (MRID 50881801[25]).

Davis Study Residue Transfer Factor: In the previous risk assessment for TCVP, it was noted that the petting/rubbing method used in this study was not conducted based entirely upon current practice for studies of this type; however, the methodology was relevant for the time at which it was conducted, and it was deemed adequate for risk quantitation. Upon comparison of the Davis study data and the recently submitted TCVP transfer study (which was conducted according to current practice), HED reevaluated the methodology used in the Davis study; specifically, the information provided regarding how the petting simulations were conducted. The study authors describe that dogs were petted by volunteers *continuously for a five-minute period* with cotton gloves. Transferable residue (petting/rubbing) samples were collected 1) from the fur of the neck (after application of the collar and rubbing over the collar), 2) from the fur of the neck (after application of the collar and then removal of the collar for sampling), and 3) along the back in the tail region after application of the collar. Two different length studies were conducted; the first study was conducted for 112 days and the second study was conducted for 12 days.

In the previous risk assessment, HED had relied on residues collected from the fur of the neck (after application of the collar and rubbing over the collar) and from the tail region. The transferable residues collected from the fur of the neck (after application of the collar and then removal of the collar for sampling) were not included since it was thought that the collection of

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[23] W. Britton. Tetrachlorvinphos: Reevaluation of "HED's Review of *Determination of the Dislodgeability of Tetrachlorvinphos (TCVP) from the Fur of Dogs Following the Application of an Insecticide Powder, Pump Spray or Aerosol*; MRID 45485501. 5/16/2014. D420285.

[24] Davis, M. et. al., *Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos*. Journal of Exposure Science and Environmental Epidemiology. (2008) 18, 564-57). D430707, W. Britton, 12/16/2015.

[25] D453149, K. Lowe et al., 12/05/2019. TCVP: Review and Summary of Residue Transfer Studies Submitted. MRID 50881801.

those residues was not consistent with the current practice for pet fur transfer residue studies. Current practice involves petting over the pet collar, assuming that the pet collar is secured in place as directed by product labeling. However, while the petting strokes should not take into account the location of the collar (i.e., the petting should not intentionally avoid the collar), they should begin from the head/neck and end at the tail (i.e., the petting stroke should not be limited to just over the neck and collar in the head/neck area). Therefore, it has been determined that the sampling in the Davis study that involved continuous rubbing over the neck and collar for five minutes likely overestimated the potential transferable residue from typical contact with a pet or what would be expected to be measured following current practice. HED has determined that the residues collected from the fur of the neck (after application and then removal of the collar for sampling) likely do not underestimate exposure considering the continuous rubbing methodology that was followed. Therefore, for the current exposure assessment for pet collars, HED has updated the calculation of the fraction transferred value by dividing the sum of the residues measured from the fur of the neck (after application of the collar and then removal of the collar for sampling) and from the back in the tail region by the amount of active ingredient in the pet collar (as reported in the Davis study), 4,800 mg. The fraction transferred proposed for non-cancer post-application risk assessment, therefore, is 0.0017 (0.17%), and is based on the mean residues reported from the 12 day study [where (8 mg + 0.08 mg)/ 4,800 mg = 0.0017]. Upon reevaluation, HED has determined that the Davis study fraction transferred and the fraction transferred determined from MRID 50881801 transfer study (described below) are similar.

MRID 50881801 Residue Transfer Factor: Hartz Mountain Corporation submitted a TCVP-specific residue transfer study for pet collars in 2019 (MRID 50881801). The purpose of the study was to measure the transferability of the test substance, TCVP, from the hair of a dog wearing a TCVP-impregnated collar. Each collar contained 14.55% TCVP (TCVP wt/collar wt). A total of 9 dogs were used in the study, randomly assigned to 3 groups. Dogs in Group 1 were petted for 5 simulations, dogs in Group 2 received 10 petting simulations, and dogs in Group 3 received 25 petting simulations. Each simulation consisted of three strokes conducted using a mannequin hand fitted with three cotton gloves. The first stroke was on the right side, the second on the left side, and the third was along the back line. Percent transferable residues of TCVP were calculated by taking the ratio of the residues of TCVP observed on the glove to the total amount of TCVP in the collar at application (calculated as the percent TCVP * initial weight of collar). This results in percent transfer values ranging from 0.049% to 0.228%. The average percent transferable residues of TCVP were 0.098% for Group 1 (5 petting simulations), 0.086% for Group 2 (10 petting simulations), and 0.167% for Group 3 (25 petting simulations). For the purpose of non-cancer post-application risk assessment, only the results from group 3 were used since that group used 25 petting simulations which most closely compares with the current methodology recommendation, which is 20 petting simulations.

Since both studies are representative of potential exposure to currently registered TCVP pet collars and provide similar estimates of transferable residue, the risk estimates presented are representative of both data sets.

A summary of the residue transfer data that has been considered for assessing exposure to TCVP pet collars is provided in Appendix G, including considerations related to the use of the Davis study and summaries of both the Davis study and MRID 50881801.

Residential Non-Cancer Post-application Exposure and Risk Equations

The algorithms used to estimate non-cancer exposure and dose for residential post-application can be found in Appendix B and the 2012 Residential SOPs.

Summary of Residential Post-Application Non-Cancer Exposure and Risk Estimates

Pet Collars: Assuming a 99.62% liquid/0.38% dust formulation ratio, the residential steady-state non-cancer incidental oral MOEs for children (1 to <2 years old) exposed to pets treated with TCVP pet collars ranged from 340 to 2,300 and are of concern (i.e., not all MOEs ≥ the LOC of 1000). Residential post-application non-cancer risk estimates for pet collars are presented in Appendix Table E.2.

Dust/Powder and Liquid Spray: Residential non-cancer incidental oral MOEs for children (1 to < 2 years old) exposed to pets treated with TCVP dust/powders range from 98 to 640 and are of concern (i.e., MOEs < the LOC of 1000). Residential non-cancer incidental oral MOEs for children (1 to < 2 years old) exposed to pets treated with TCVP liquid spray products range from 1,600 to 15,000 and are not of concern (i.e., MOEs ≥ the LOC of 1000). Residential post-application non-cancer risk estimates for dust/powders and liquid sprays are presented in Appendix Table E.3.

Residential Cancer Post-Application Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential cancer post-application risk assessment.

Dust/Powder and Liquid Spray Transfer Data: For the purpose of quantification of estimated TCVP post-application cancer exposures/risks, HED used the average percent residue transfer from the available TCVP dust/powder and liquid spray studies. HED used an average of the maximum observed percent residue transfer for each day tested for calculation of cancer exposures/risks resulting in a fraction transferred of 0.022% and 0.18% for dusts/powders and liquid sprays, respectively.

Pet Collar Transfer Data: For the assessment of cancer post-application risks, longer-term residue transfer values from the Davis study (from the 112 day study) were used to best represent the assumption of 180 days/year exposure for cancer assessment. As noted above for the non-cancer estimate, HED had previously included the residues from the fur of the neck (after application of the collar and rubbing over the collar) in the calculation of the fraction transferred. Updated calculations using residues from the fur of the neck (after application of the collar and then removal of the collar for sampling) were conducted for the cancer post-application risk assessment, resulting in a revised fraction transfer of 0.00092 (0.09%), based on the mean residues (112 days) in the Davis study [where (4.3 mg + 0.13)/ 4,800 mg = 0.00092].

Days per Year of Exposure:

For the purpose of estimating adult dermal cancer risks, exposure was assumed for 180 of 365 total days per year. This factor is used as a health protective estimate of the number of days that an individual could be exposed to a treated animal per year of product use. The recommendation

of 6 months exposure is conservative, particularly when paired with the assumption that this exposure duration is repeated for 50 years during an adult's lifetime.

Years per Lifetime of Exposure:
It is assumed that adults would be exposed for 50 years out of a 78 year lifespan. This factor is routinely used as a conservative estimate of the number of years an individual could continually use a single pesticide product.

Lifetime Expectancy: Life expectancy values are from the Exposure Factors Handbook 2011 Edition Table 18-1 (U.S. EPA, 2011[26]). The table shows that the overall life expectancy is 78 years based on life expectancy data from 2007. In 2007, the average life expectancy for males was 75 years and 80 years for females. Based on the available data, the recommended value for use in cancer risk assessments is 78 years.

Residential Cancer Post-application Exposure and Risk Estimate Equations

As was done for residential handlers, cancer post-application risk estimates for adults were calculated using a linear low-dose extrapolation approach in which a LADD is first calculated and then compared with a Q_1^* that has been calculated for TCVP based on dose response data in the appropriate toxicology study ($Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$). The algorithms used to estimate the LADD and cancer risk for residential post-application exposure can be found in Appendix B.

Summary of Residential Post-application Cancer Exposure and Risk Estimates

Pet Collars: Assuming a 99.62% liquid/0.38% dust formulation ratio, residential post-application cancer (adult only) risk estimates for TCVP pet collars range from 10^{-7} to 10^{-6}. Residential post-application cancer risk estimates for pet collars are presented in Appendix Table F.1.

Dust/Powder and Liquid Spray: Residential post-application cancer (adult only) risks estimated for TCVP dust/powder products range from 10^{-7} to 10^{-6}, and for TCVP liquid sprays are all 10^{-7}. Residential post-application cancer risk estimates for dust/powders and liquid sprays are presented in Appendix Table F.2.

[26] https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252.

Appendix A – Summary of TCVP Pet Product Labels and Use Directions

Table A.2. Summary of TCVP Pet Products.			
EPA Reg. No.	Use Site	Application Rate	Use Restrictions
Collars			
2596-49 (collar weight: 11.3 g)	Cats	11.3 gram collar (14.6 % ai) Total ai: 0.0036 lb ai or 1,650 mg ai 20% removed: 1,320 mg ai	Do not use in kittens under 12 weeks of age. Place the collar around the cat's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 3 months, every 2 months for severe infestation.
2596-50 (collar weight: 19 g) 2596-62 (collar weight: 19 – 32 g)	Dogs	19 gram collar (14.6 % ai) Total ai: 0.0061 lb ai or 2,774 mg ai 20% removed: 2,219 mg ai 32 gram collar (14.6 % ai) Total ai: 0.0103 lb ai or 4,672 mg ai 20% removed: 3,738 mg ai	Do not use on puppies less than 6 weeks of age. Place the collar around the dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 3 months, every 2 months for severe infestation.
2596-63 (collar weight: 15 – 17 g)	Cats	15 gram collar (14.6% ai) Total ai: 0.0048 lb ai or 2,190 mg ai 20% removed: 1,752 mg ai 17 gram collar (14.6% ai) Total ai: 0.0055 lb ai or 2,482 mg ai 20% removed: 1,986 mg ai	Do not use on kittens less than 12 weeks of age. Place the collar around the cat's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 5 months, every 4 months for severe infestation.
2596-83 (collar weight: 12 – 25 g)	Cats	12 gram collar (14.6% ai) Total ai: 0.0039 lb ai or 1,752 mg ai 20% removed: 1,402 25 gram collar (14.6% ai) Total ai: 0.0080 lb ai or 3,650 mg ai 20% removed: 2,920 mg ai	Do not use on kittens less than 12 weeks of age. Place the collar around the cat's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 7 months, every 5 months for severe infestation.
2596-84 (collar weight: 19 – 32 g)	Dogs	19 gram collar (14.6% ai) Total ai: 0.0061 lb ai or 2,774 mg ai 20% removed: 2,219 mg ai 32 gram collar (14.6% ai) Total ai: 0.0103 lb ai or 4,672 mg ai 20% removed: 3,738 mg ai	Do not use on puppies under 6 weeks of age. Place the collar around the dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 7 months, every 5 months for severe infestation.
2596-139 (collar weight: 10 – 50 g[1]; assumed lower end of range for cats)	Cats	10 gram collar (14.6% ai) Total ai: 0.0032 lb ai or 1,460 mg ai 20% removed: 1,168 mg ai	Do not use on puppies under 6 weeks old/ kittens under 12 weeks old. Place the collar around the cat's/dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 7 months, or more frequently for severe infestation.

Table A.2. Summary of TCVP Pet Products.			
EPA Reg. No.	Use Site	Application Rate	Use Restrictions
2596-139 (collar weight: 10 – 50 g[1]; assumed high end of range for dogs)	Dogs	50 gram collar (14.6% ai) Total ai: 0.0161 lb ai or 7,300 mg ai 20% removed: 5,840 mg ai	Do not use on puppies under 6 weeks old/ kittens under 12 weeks old. Place the collar around the cat's/dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 7 months, or more frequently for severe infestation.
Dusts/Powders			
2596-78	Cats	0.3 ounce of powder for a small cat or 0.5 ounce for a large cat (3.3% ai) Small cat: 8.5 grams product = 0.00062 lb ai or 280.5 mg ai Large cat: 14.2 grams product = 0.00103 lb ai or 468.6 mg ai	Not for use on kittens less than 12 weeks of age. Dust entire cat beginning at head and working back. Use approximately 1/3 ounce of powder for a small cat or ½ ounce for a large cat. Repeat at weekly intervals if necessary.
2596-79	Dogs	0.5 ounce of powder for a small dog; 1 oz for a medium dog; and 1.25 oz for large dogs (3.3% ai) Small: 14.2 grams product = 0.00103 lb ai or 468.6 mg ai Medium: 28.4 grams product = 0.00206 lb ai or 937.2 mg ai Large: 35.5 grams product = 0.00258 lb ai or 1171.5 mg ai	Not for use on puppies less than 12 weeks of age. Dust entire dog beginning at the head and working back. Make sure powder gets down to the skin. Lightly dust the dog's bedding with approximately the same amount of powder. Repeat treatment of dog and bedding at weekly intervals if necessary. Use ½ ounce of powder for a small dog; 1 oz for a medium dog; and 1 ¼ oz for large dogs.
47000-123	Cats	0.3 oz (8.5 grams) of powder per every 10 pounds of body weight (1.0% ai) Estimated Range: Small (5 lbs): 4.25 grams product = 0.00009 lb ai or 42.5 mg ai Medium (12 lbs): 10.2 grams product = 0.00022 lb ai or 102 mg ai Large (18 lbs): 15.3 grams product = 0.00034 lb ai or 153 mg ai, large	Do not apply to kittens or puppies under 12 weeks old. Dust powder evenly over the animal and rub thoroughly through the hair coat to skin. Use 1/3 oz (8.5 grams) of powder per every 10 pounds of body weight of your cat or dog. Do not reapply product for 30 days. *PPE: Baseline clothing, coveralls, gloves and dust mist respirator.
	Dogs	1/3 oz (8.5 grams) of powder per every 10 pounds of body weight (1.0% ai) Estimated Range: Small (20 lbs): 17 grams product = 0.00037 lb ai or 170 mg ai Medium (50 lbs): 42.5 grams product = 0.00094 lb ai or 425 mg ai Large (80 lbs): 68 grams product = 0.0015 lb ai or 680 mg ai	
Liquid (Pump/Trigger) Sprays[2]			
2596-125	Dogs (Trigger)	1.1% ai Small: 30 strokes = 27.78 grams product = 0.00066 lb ai or 300 mg ai Medium: 40 strokes = 37.04 grams product = 0.00088 lb ai or 400 mg ai Large: 70 strokes = 64.82 grams product = 0.0015 lb ai or 700 mg ai, large	Do not apply to pets (puppies) less than 6 weeks old. Hold bottle upright about 6 inches from pet. Spray lightly until the tips of the pet's hair are moist. Rub spray into animal's coat. Repeat once per week. Recommended dosage: Spray 25-30 strokes for a small dog. Spray 30-40 strokes for a medium dog. Spray 40-70 strokes for a large dog. More spray may be needed for longhaired dogs.[3]

Table A.2. Summary of TCVP Pet Products.			
EPA Reg. No.	Use Site	Application Rate	Use Restrictions
2596-126	Cats (Trigger)	1.1% ai Small: 25 strokes = 23.15 grams product = 0.00055 lb ai or 250 mg ai Large: 35 strokes = 32.41 grams product = 0.00077 lb ai or 350 mg ai	Do not apply to pets (kittens) less than 6 weeks old. Hold bottle upright about 6 inches from pet. Spray lightly until the tips of the pet's hair are moist. Rub spray into animal's coat. Repeat once per week. Recommended dosage: Spray 15-25 strokes for a small cat. Spray 25-35 strokes for a large cat. More spray may be needed for longhaired cats.[3]
2596-140	Cats[5] (Pump)	1.1% ai Small: 25 strokes = 4.73 grams product = 0.00011 lb ai or 51 mg ai Large: 35 strokes = 6.62 grams product = 0.00016 lb ai or 71 mg ai	Do not use on puppies or kittens less than 12 weeks old. Hold bottle upright about 6 inches from pet. Spray lightly until the tips of the pet's hair are moist. Rub spray into animal's coat. Repeat once per week. Recommended dosage: Spray 15-25 strokes for a small cat. Spray 25-35 strokes for a large cat.[4] Recommended dosage: Spray 25-35 strokes for a small dog. Spray 30-40 strokes for a medium dog. Spray 40-70 strokes for a large dog.[4]
	Cats[5] (Trigger)	1.1% ai Small: 25 strokes = 23.15 grams product = 0.00055 lb ai or 250 mg ai Large: 35 strokes = 32.41 grams product = 0.00077 lb ai or 350 mg ai	
	Dogs (Trigger)	1.1% ai Small: 35 strokes = 32.41 grams product = 0.00077 lb ai or 350 mg ai Medium: 40 strokes = 37.04 grams product = 0.00088 lb ai or 400 mg ai Large: 70 strokes = 64.82 grams product = 0.0015 lb ai or 700 mg ai	

1. This product (EPA Reg. #2696-139) is approved for both cats and dogs, and only one range of collar weights is provided on the label. Therefore, HED has assumed that the low end of that range would be appropriate for cats and the high end of that range would be appropriate for dogs.
2. Application rates for liquid spray products determined using information provided by the Registrant regarding the volume of product released per stroke: pump spray products = 0.19 g and trigger-spray products = 0.93 g.
3. Current label language (EPA Reg. No. 2596-125 and 2596-126) allows for more than a prescribed amount of strokes per cat/dog. Assessment is based on the amount labelled for each weight range. Any such label language allowing for an exceedance should be removed.
4. The recommended number of strokes as presented for EPA Reg. No. 2596-140 is based on master label amendments proposed by the registrant and granted by EPA (March 2014). Previously, a number of strokes per cat/dog was not recommended. The maximum number of strokes was considered in the risk assessment for cats and dogs based on animal size.
5. EPA Reg. No. 2596-140 registered as both a pump spray and trigger spray for cats.

Appendix B: Summary of Residential Non-cancer Algorithms

Residential Dermal and Inhalation Handler Exposure Algorithm

Daily dermal and inhalation exposure (mg/day) for residential pesticide handlers, for a given formulation-application method combination, is estimated by multiplying the formulation-application method-specific unit exposure by an estimate of the amount of active ingredient handled in a day, using the equation below:

$$E = UE * AR * A$$

where:

E = exposure (mg/day);
UE = unit exposure (mg/lb ai);
AR = application rate (e.g., lb ai/ft^2, lb ai/gal); and
A = number of animals treated per day.

Residential Post-application Dermal Exposure Algorithm

The following method is used to calculate dermal exposures that are attributable to an adult or child contacting a treated companion pet:

$$E = TC * TR * ET$$

where:

E = exposure (mg/day);
TC = transfer coefficient (cm^2/hr);
TR = transferable residue (mg/cm^2); and
ET = exposure time (hours/day).

$$TR = \frac{AR * F_{AR}}{SA}$$

where:

TR = transferable residue (mg/cm^2);
AR = application rate or amount applied to animal (mg);
F_{AR} = fraction of the application rate available as transferable residue; and
SA = surface area of the pet (cm^2).

Absorbed dermal dose, normalized to body weight, is calculated as:

$$D = \frac{E * AF}{BW}$$

where:

D = dose (mg/kg-day);
E = exposure (mg/day);
AF = absorption factor (dermal); and
BW = body weight (kg).

Table B.1. Treated Pets – Inputs for Residential Post-application Dermal Exposure			
Algorithm Notation	Exposure Factor Units		Point Estimates
AR	Application rate (mg)		Unique for each product
SA	Surface Area of Animal (cm^2)	Small Cat, Dog	Cat – 1,500 Dog – 3,000
		Medium Cat, Dog	Cat – 2,500 Dog – 7,000
		Large Cat, Dog	Cat – 4,000 Dog – 11,000
F_{AR}	Fraction of AR Available for Transfer (recommended point estimate)		Non-Cancer Collar (MRID 50881801): 0.0017 Collar (Davis study): 0.0017 Dust/Powder (TCVP): 0.00048 Pump Spray (TCVP): 0.0081 Cancer Collar (Davis study): 0.00092 Dust/Powder (TCVP): 0.00022 Pump Spray (TCVP): 0.0018
TC	Transfer Coefficient – Liquids (cm^2/hr)	Adult	5,200
		Children 1 < 2 years old	1,400
	Transfer Coefficient – Solids (cm^2/hr)	Adult	140,000
		Children 1 < 2 years old	38,000
ET	Exposure Time (hours per day)	Adult	0.77
		Children 1 < 2 years old	1.0
BW	Body weight (kg)	Adult	80
		Children 1 < 2 years old	11

Residential Post-application Hand-to-Mouth Exposure Algorithm

Exposure from hand-to-mouth activity is calculated as follows (based on algorithm utilized in SHEDS-Multimedia):

$$E = [HR * (F_M * SA_H) * (ET * N\_Replen) * (1 - (1 - SE)^{(Freq\_HtM/N\_Replen)})]$$

where:

E = exposure (mg/day);
HR = hand residue loading (mg/cm^2);
SA_H = surface area of one child hand (cm^2);
F_M = fraction hand surface area mouthed /event (fraction/event);
ET = exposure time (hr/day);
N_Replen = number of replenishment intervals per hour (intervals/hour);
SE = saliva extraction factor (i.e., mouthing removal efficiency); and
Freq_HtM = number of hand-to-mouth contacts events per hour (events/hour).

and

$$HR = \frac{E * Fai_{hands}}{2 * SA_H}$$

where:
HR = hand residue loading (mg/cm^2);
E = dermal exposure (mg);
Fai_{hands} = fraction of a.i. on hands compared to total residue from dermal transfer coefficient study (unitless); and
SA_H = surface area of one child hand (cm^2).

Oral dose, normalized to body weight, is calculated as:

$$D = \frac{E}{BW}$$

where:
D = dose (mg/kg-day);
E = exposure (mg/day); and
BW = body weight (kg).

Table B.2. Treated Pets – Inputs for Residential Post-application Hand-to-Mouth Exposure

Algorithm Notation	Exposure Factor (units)		Point Estimate(s)
Fai_{hands}	Fraction of a.i. on hands from transfer coefficient studies (unitless)		Solid = 0.37 Liquid = 0.040
F_M	Fraction hand surface area mouthed /event (fraction/event)		0.13
N_Replen	Replenishment intervals per hour (intervals/hr)		4
ET	Exposure time (hours/day)	Children 1 < 2 years old	1.0
SE	Saliva extraction factor		0.48
Freq_HtM	Hand-to-mouth events per hour (events/hr)	Children 1 < 2 years old	20
SA_H	Typical surface area of one child hand (cm^2)	Children 1 < 2 years old	150
BW	Body Weight (kg)	Children 1 < 2 years old	11

Residential Cancer Algorithms

After the development of the ADD values, the next step required to calculate carcinogenic risk estimates is to amortize these values over the anticipated lifetime, which results in the LADD. LADD values are calculated using the following equation:

$$LADD = ADD * \frac{Days\ per\ Year\ of\ Exposure}{365\ Days\ per\ Year} * \frac{Years\ per\ Lifetime\ of\ Exposure}{Lifetime\ Expectancy}$$

where:

LADD	=	absorbed dose over a lifetime (mg ai/kg/day),
ADD	=	average daily dose absorbed in a given scenario (mg ai/kg/day),
Days per Year of Exposure	=	annual frequency of an application by an individual (days/year),
Years per Lifetime of Exposure	=	amount of a lifetime that an individual would be expected to use pesticides (years), and
Lifetime Expectancy	=	average life expectancy of an individual (years).

Cancer risk estimate calculations are completed by comparing the LADD values calculated above to the Q_1* for the chemical. Cancer risk estimates are calculated using the following equation:

$$Total\ Cancer\ Risk\ Estimate = (Dermal\ LADD + Inhalation\ LADD) * Q_1*$$

where:

Cancer Risk Estimate	=	probability of incidence of cancer cases over a lifetime (unitless),
Dermal LADD	=	absorbed dose from dermal exposure over a lifetime (mg ai/kg/day),
Inhalation LADD	=	absorbed dose from inhalation exposure over a lifetime (mg ai/kg/day), and
Q_1*	=	quantitative dose response factor used for linear, low-dose response cancer risk estimate calculations $(mg/kg/day)^{-1}$.

Table B.3. Treated Pets – Inputs for Cancer Exposure/Risk

Algorithm Notation	Exposure Factor (units)	Point Estimate(s)
EF	Exposure Frequency (days/year)	Residential: Handlers - Collars, 4 Dusts/Powders and Liquid Sprays, 6 Post-application (all formulations) - 180
ET	Exposure Time (years)	50: residential
AT	Averaging Time (years)	78
CF	Conversion Factor (days/year)	365

Appendix C – Summary of Residential Handler Non-Cancer Exposures and Risks

Table C.1. Residential Handler Non-Cancer Dermal and Inhalation Doses Assuming a Liquid or Dust Formulation for Pet Collars.
Table C.2. Residential Handler Non-Cancer Risk Estimates from Use of TCVP Pet Collars Assuming 99.62% Liquid/0.38% Dust Ratio Formulation.
Table C.3. Residential Handler Non-Cancer Risk Estimates from Use of TCVP Dust/Powder and Liquid Spray Products.

Table C.1. Residential Handler Non-Cancer Dermal and Inhalation Doses Assuming a Liquid or Dust Formulation for Pet Collars.

Exposure Scenario	Reg. No. (Target Animal)	Animal Type	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (mg/lb ai)	Maximum Application Rate[1] (lb ai/pet)	Amount Handled Daily (animals treated per day)[2]	Dermal Dose (mg/kg/day)[3]	Inhalation Dose (mg/kg/day)[4]
	Assume Liquid Formulation -- Use of Spot-On Exposure Data (based on 2012 Residential SOPs)							
Application of TCVP Collars	2596-49 (Cat)	All	120	Negligible	0.0036	2	0.0012	Negligible
	2596-50, 62 (Dog)	Small			0.0061		0.0020	
		Large			0.0103		0.0034	
	2596-63 (Cat)	Small			0.0048		0.0016	
		Large			0.0055		0.0018	
	2596-83 (Cat)	Small			0.0039		0.0013	
		Medium			0.0059		0.0020	
		Large			0.0080		0.0027	
	2596-84 (Dog)	Small			0.0061		0.0021	
		Large			0.0103		0.0034	
	2596-139 (Cat)	All			0.0032		0.0011	
	2596-139 (Dog)	All			0.0161		0.0054	
	Assume Dust Formulation -- Use of TCVP Dust Applicator Exposure Data (MRID 45519601)							
Application of TCVP Collars	2596-49 (Cat)	All	1,700	3.1	0.0036	2	0.017	0.00033
	2596-50, 62 (Dog)	Small			0.0061		0.029	0.00055
		Large			0.0103		0.049	0.00092
	2596-63 (Cat)	Small			0.0048		0.023	0.00043
		Large			0.0055		0.026	0.00049
	2596-83 (Cat)	Small			0.0039		0.018	0.00035
		Medium			0.0059		0.028	0.00053
		Large			0.0080		0.038	0.00072
	2596-84 (Dog)	Small			0.0061		0.029	0.00055
		Large			0.0103		0.049	0.00092
	2596-139 (Cat)	All			0.0032		0.015	0.00029

Table C.1. Residential Handler Non-Cancer Dermal and Inhalation Doses Assuming a Liquid or Dust Formulation for Pet Collars.								
Exposure Scenario	Reg. No. (Target Animal)	Animal Type	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (mg/lb ai)	Maximum Application Rate[1] (lb ai/pet)	Amount Handled Daily (animals treated per day)[2]	Dermal Dose (mg/kg/day)[3]	Inhalation Dose (mg/kg/day)[4]
	2596-139 (Dog)	All			0.0161		0.076	0.00144

1 Based on registered TCVP pet product labels (see Table A2). Application rate (lb ai/pet) = (collar weight in grams ÷ 454 lb/g conversion factor) * percent ai in collar.
2 Based on HED's 2012 Residential SOPs (http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide).
3 Dermal Dose = Dermal Unit Exposure (mg/lb ai) × Application Rate (lb ai/pet) × Area Treated or Amount Handled (pets/day) × Dermal Absorption Factor (9.6 %) ÷ Body Weight (69 kg).
4 Inhalation Dose = Inhalation Unit Exposure (mg/lb ai) × Application Rate (lb ai/pet) × Area Treated or Amount Handled (pets/day) ÷ Body Weight (69 kg).

Table C.2. Residential Handler Non-Cancer Risk Estimates from Use of TCVP Pet Collars Assuming 99.62% Liquid/0.38% Dust Ratio Formulation. LOC = 300							
Exposure Scenario	Reg. No. (Target Animal)	Animal Type	Maximum Application Rate[1] (lb ai/pet)	Amount Handled Daily (animals treated per day)[2]	Combined 99.62%/0.38% Liquid/Dust Dermal Dose (mg/kg/day)[3]	Combined 99.62%/0.38% Liquid/Dust Inhalation Dose (mg/kg/day)[4]	Combined 99.62%/0.38% Liquid/Dust Ratio Inhalation MOE **(LOC = 300)**[5]
Application of TCVP Collars	2596-49 (Cat)	All	0.0036	2	0.0013	0.0000012	1,100,000
	2596-50, 62 (Dog)	Small	0.0061		0.0021	0.0000021	630,000
		Large	0.0103		0.0036	0.0000035	370,000
	2596-63 (Cat)	Small	0.0048		0.0017	0.0000016	800,000
		Large	0.0055		0.0019	0.0000019	700,000
	2596-83 (Cat)	Small	0.0039		0.0013	0.0000013	990,000
		Medium	0.0059		0.0021	0.0000020	640,000
		Large	0.0080		0.0028	0.0000027	480,000
	2596-84 (Dog)	Small	0.0061		0.0022	0.0000021	630,000
		Large	0.0103		0.0036	0.0000035	370,000
	2596-139 (Cat)	All	0.0032		0.0011	0.0000011	1,200,000
	2596-139 (Dog)	All	0.0161		0.0056	0.0000055	240,000

1 Based on registered TCVP pet product labels (see Table A2). Application rate (lb ai/pet) = (collar weight in grams ÷ 454 lb/g conversion factor) * percent ai in collar.
2 Based on HED's 2012 Residential SOPs (http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide).
3 Combined 99.62%/0.38% Liquid/Dust Dermal Dose = (Liquid dermal dose * 0.9962) + (Dust dermal dose * 0.0038).
4 Combined 99.62%/0.38% Liquid/Dust Inhalation Dose = (Liquid inhalation dose * 0.9962) + (Dust inhalation dose * 0.0038).
5. No dermal MOE estimated due to lack of dermal hazard. Inhalation MOE = Inhalation HED (1.31 mg/kg/day) ÷ Combined 99.62%/0.38% Liquid/Dust Inhalation Dose (mg/kg/day).

Table C.3. Residential Handler Non-Cancer Risk Estimates from Use of TCVP Dust/Powder and Liquid Spray Products.

Exposure Scenario	Reg. No. (Target Animal)	Type of Animal	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (mg/lb ai)	Maximum Application Rate[1] (lb ai/pet)	Amount Handled Daily (animals treated per day)[2]	Dermal		Inhalation	
							Dose (mg/kg/day)[3]	MOE[4]	Dose (mg/kg/day)[5]	MOE **(LOC = 300)[6]**
Application of TCVP Dusts/Powders	47000-123 (Dog)	Small	1,700	3.1	0.00037	2	0.0018	N/A, No Dermal Hazard	0.000034	39,000
		Medium			0.00094		0.0044		0.000084	16,000
		Large			0.0015		0.0071		0.00013	9,700
	47000-123 (Cat)	Small			0.000094		0.00044		0.0000084	160,000
		Medium			0.00023		0.0011		0.000020	65,000
		Large			0.00034		0.0016		0.000030	43,000
	2596-78 (Cat)	Small			0.00062		0.0029		0.000056	24,000
		Large			0.0010		0.0049		0.000093	14,000
	2596-79 (Dog)	Small			0.0010		0.0049		0.000093	14,000
		Medium			0.0021		0.0097		0.00019	7,100
		Large			0.0026		0.0122		0.00023	5,600
Application of TCVP Liquid (Pump/Trigger) Sprays	2596-126, -140 (Cat) (Trigger)	Small	820	3.3	0.00055		0.0013	N/A, No Dermal Hazard	0.000053	25,000
		Large			0.00077		0.0018		0.000074	18,000
	2596-140 (Cat) (Pump)	Small			0.00011		0.00026		0.000011	120,000
		Large			0.00016		0.00036		0.000015	87,000
	2596-125, -140 (Dog) (Trigger)	Small			0.00077		0.0018		0.000074	18,000
		Medium			0.00088		0.0020		0.000084	16,000
		Large			0.0015		0.0035		0.00015	8,900

1 Based on registered TCVP pet product labels.

2 Based on HED's 2012 Residential SOPs (http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide)

3 Dermal Dose = Dermal Unit Exposure (mg/lb ai) × Application Rate (lb ai/pet) × Area Treated or Amount Handled (pets/day) × Dermal Absorption Factor (9.6%) ÷ Body Weight (69 kg). Dermal dose presented only for purpose of calculation of cancer risks for residential handlers.

4 No dermal MOE estimated due to lack of dermal hazard.

5 Inhalation Dose = Inhalation Unit Exposure (mg/lb ai) × Application Rate (lb ai/pet) × Area Treated or Amount Handled (pets/day) ÷ Body Weight (69 kg).

6 Inhalation MOE = Inhalation HED (1.31 mg/kg/day) ÷ Inhalation Dose (mg/kg/day).

Appendix D – Summary of Residential Handler Cancer Exposure and Risk Estimates

Table D.1. Residential Handler Cancer Risk Estimates from Use of TCVP Pet Collars Assuming 99.62% Liquid/0.38% Dust Ratio Formulation.

Table D.2. Residential Handler Cancer Risk Estimates from Use of TCVP Dust/Powder and Liquid Spray Products.

Table D.1. Residential Handler Cancer Risk Estimates from Use of TCVP Pet Collars Assuming 99.62% Liquid/0.38% Dust Ratio Formulation.

Reg No./ Animal Type	Animal Size	Lifestage	Liquid LADD[1]	Dust LADD[2]	99.62% Liquid / 0.38% Dust Cancer Risk Estimate[3]
2596-49 (Cat)	Any	Adult	8.5E-06	1.2E-04	1.6E-08
2596-50, 62 (Dog)	Small		1.4E-05	2.1E-04	2.7E-08
	Large		2.4E-05	3.5E-04	4.6E-08
2596-63 (Cat)	Small		1.1E-05	1.6E-04	2.2E-08
	Large		1.3E-05	1.8E-04	2.5E-08
2596-83 (Cat)	Small		9.0E-06	1.3E-04	1.7E-08
	Medium		1.4E-05	2.0E-04	2.7E-08
	Large		1.9E-05	2.7E-04	3.6E-08
2596-84 (Dog)	Small		1.4E-05	2.1E-04	2.8E-08
	Large		2.4E-05	3.5E-04	4.6E-08
2596-139 (Cat)	Any		7.5E-06	1.1E-04	1.4E-08
2596-139 (Dog)	Any		3.8E-05	5.4E-04	7.2E-08

1 Liquid LADD = [Inhalation + Dermal Dose (mg/kg/day)] × [Days per year of exposure (4 days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (50 yrs) ÷ Lifetime expectancy (78 yrs)]. Inhalation exposures considered negligible based on use of spot-on data for liquid pet collar formulation.

2 Dust LADD = [Inhalation + Dermal Dose (mg/kg/day)] × [Days per year of exposure (4 days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (50 yrs) ÷ Lifetime expectancy 78 (yrs)].

3 Cancer risk estimates = [(Liquid LADD * 0.9962) + (Dust LADD * 0.0038)] × Q_1^*, where $Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$

Table D.2. Residential Handler Cancer Risk Estimates from Use of TCVP Dust/Powder and Liquid Spray Products.

Reg No./ Animal Type	Animal Size	Lifestage	Total LADD[1,2]	Cancer Risk Estimate[3]
Dust/Powder				
47000-123 (Dog)	Small	Adult	1.9E-05	3.5E-08
	Medium		4.7E-05	8.7E-08
	Large		7.6E-05	1.4E-07
47000-123 (Cat)	Small		4.7E-06	8.7E-09
	Medium		1.1E-05	2.1E-08
	Large		1.7E-05	3.1E-08
2596-78 (Cat)	Small		3.1E-05	5.7E-08
	Medium		5.2E-05	9.6E-08
2596-79 (Dog)	Small		5.2E-05	9.6E-08
	Medium		1.0E-04	1.9E-07
	Large		1.3E-04	2.4E-07
Liquid (Pump/Trigger) Sprays				
2596-126, -140 (Cat) (Trigger)	Small	Adult	1.4E-05	2.5E-08
	Large		1.9E-05	3.5E-08
2596-140 (Cat) (Pump)	Small		2.8E-06	5.1E-09
	Large		3.9E-06	7.2E-09
2596-125, -140 (Dog) (Trigger)	Small		1.9E-05	3.5E-08
	Medium		2.2E-05	4.0E-08
	Large		3.9E-05	7.0E-08

1 Total Lifetime Average Daily Dose (LADD, mg/kg/day) = Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day).

2 Dermal and Inhalation LADD equations provided in Appendix B.

3 Cancer risk estimates = Total LADD × Q_1^*, where $Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$

Appendix E – Summary of Residential Post-Application Non-Cancer Exposure and Risk Estimates

Table E.1. Residential Post-application Non-cancer Incidental Oral Dose Assuming a Liquid or Dust Formulation for Pet Collars.
Table E.2. Residential Post-Application Non-Cancer Risk Estimates from Use of TCVP Pet Collars Assuming 99.62% Liquid/0.38% Dust Ratio Formulation.
Table E.3. Residential Post-Application Non-Cancer Risk Estimates from Use of TCVP Dust/Powder and Liquid Spray Formulations.

Table E.1. Residential Post-application Non-cancer Incidental Oral Dose Assuming a Liquid or Dust Formulation for Pet Collars.

Animal Type	Animal Size	Application Rate (mg ai)[1]	F_{ahands}	DE	SA_H	HR	F_{ss}	ET	Replenishment interval (min)	N_Replen	SE	Freq_HtM	Incidental oral Absorbed Dose[3] (mg/kg/day)
				Dermal Exposure (mg)[2]	Surface area of 1 hand (cm^2)	Hand residue loading (mg/cm^2)	Fraction of hand mouthed	Exposure Time (hours/day)		# replenishment intervals per hour (intervals/hr)	Fraction Saliva Extraction	Number of hand-to-mouth contacts events per hour (events/hr)	
Assume Liquid Formulation													
Cat (2596-49)	small	1,320	0.04	2.1	150	0.0003	0.13	1	15	4	0.48	20	0.0019
	medium	1,320	0.04	1.3	150	0.0002	0.13	1	15	4	0.48	20	0.0011
	large	1,320	0.04	0.8	150	0.0001	0.13	1	15	4	0.48	20	0.0007
Dog (2596-50,62)	small	2,219	0.04	1.8	150	0.0002	0.13	1	15	4	0.48	20	0.0016
	large	3,738	0.04	0.8	150	0.0001	0.13	1	15	4	0.48	20	0.0007
Cat (2596-63)	small	1,752	0.04	2.8	150	0.0004	0.13	1	15	4	0.48	20	0.0025
	large	1,986	0.04	1.2	150	0.0002	0.13	1	15	4	0.48	20	0.0011
Cat (2596-83)	small	1,402	0.04	2.2	150	0.0003	0.13	1	15	4	0.48	20	0.0020
	medium	2,161	0.04	2.1	150	0.0003	0.13	1	15	4	0.48	20	0.0019
	large	2,920	0.04	1.7	150	0.0002	0.13	1	15	4	0.48	20	0.0016
Dog (2596-84)	small	2,219	0.04	1.8	150	0.0002	0.13	1	15	4	0.48	20	0.0016
	large	3,738	0.04	0.8	150	0.0001	0.13	1	15	4	0.48	20	0.0007
Cat (2596-139)	small	1,168	0.04	1.9	150	0.0002	0.13	1	15	4	0.48	20	0.0017
	medium	1,168	0.04	1.1	150	0.0001	0.13	1	15	4	0.48	20	0.0010
	large	1,168	0.04	0.7	150	0.00009	0.13	1	15	4	0.48	20	0.0006
Dog (2596-139)	small	5,840	0.04	4.6	150	0.0006	0.13	1	15	4	0.48	20	0.0042
	medium	5,840	0.04	2.0	150	0.0003	0.13	1	15	4	0.48	20	0.0018
	large	5,840	0.04	1.3	150	0.0002	0.13	1	15	4	0.48	20	0.0011
Assume Dust Formulation													
Cat (2596-49)	small	1,320	0.37	57	150	0.0701	0.13	1	15	4	0.48	20	0.48
	medium	1,320	0.37	34	150	0.0421	0.13	1	15	4	0.48	20	0.29
	large	1,320	0.37	21	150	0.0263	0.13	1	15	4	0.48	20	0.18
Dog (2596-50,62)	small	2,219	0.37	48	150	0.0589	0.13	1	15	4	0.48	20	0.40
	large	3,738	0.37	22	150	0.0271	0.13	1	15	4	0.48	20	0.18
Cat (2596-63)	small	1,752	0.37	75	150	0.0931	0.13	1	15	4	0.48	20	0.63
	large	1,986	0.37	32	150	0.0395	0.13	1	15	4	0.48	20	0.27
Cat (2596-83)	small	1,402	0.37	60	150	0.0744	0.13	1	15	4	0.48	20	0.51
	Medium	2,161	0.37	56	150	0.0689	0.13	1	15	4	0.48	20	0.47
	large	2,920	0.37	47	150	0.0582	0.13	1	15	4	0.48	20	0.40

Table E.1. Residential Post-application Non-cancer Incidental Oral Dose Assuming a Liquid or Dust Formulation for Pet Collars.													
Animal Type	Animal Size	Application Rate (mg ai)[1]	$F_{ai_{hands}}$	DE Dermal Exposure (mg)[2]	SA_H Surface area of 1 hand (cm^2)	HR Hand residue loading (mg/cm^2)	F_m Fraction of hand mouthed	ET Exposure Time (hours/day)	Replenish-ment interval (min)	N Replen # replenish-ment intervals per hour (intervals/hr)	SE Fraction Saliva Extraction	Freq HtM Number of hand-to-mouth contacts events per hour (events/hr)	Incidental oral Absorbed Dose[3] (mg/kg/day)
Dog (2596-84)	small	2,219	0.37	48	150	0.0589	0.13	1	15	4	0.48	20	0.40
	large	3,738	0.37	22	150	0.0271	0.13	1	15	4	0.48	20	0.18
Cat (2596-139)	small	1,168	0.37	50	150	0.0620	0.13	1	15	4	0.48	20	0.42
	medium	1,168	0.37	30	150	0.0372	0.13	1	15	4	0.48	20	0.25
	large	1,168	0.37	19	150	0.0233	0.13	1	15	4	0.48	20	0.16
Dog (2596-139)	small	5,840	0.37	126	150	0.1551	0.13	1	15	4	0.48	20	1.06
	medium	5,840	0.37	54	150	0.0665	0.13	1	15	4	0.48	20	0.45
	large	5,840	0.37	34	150	0.0423	0.13	1	15	4	0.48	20	0.29

1. Application rates are label defined and adjusted for 20% removal of the pet collar. Refer to Table A.2.
2. Dermal Exposure (mg/day) = [Transfer Coefficient (cm^2/hr)] * [Application Rate (label defined) * Fraction Application Rate (0.0017; Davis, M. et. al and MRID 50881801) ÷ Surface Area of Cat/Dog (Cat: Small, 1,500; Medium, 2,500; Large, 4,000 cm^2 - Dog: Small, 3,000; Medium, 7,000; Large, 11,000 cm^2)] x [Exposure Time (Adults, 0.77 hours/day; Children, 1.0 hours/day))
3. Incidental Oral Dose (mg/kg/day) = [Hand Residue Loading (mg/cm^2)] × [Fraction of Hand Mouthed (0.13) × Surface Area of 1 Child Hand (150 cm^2)] x [Exposure Time (1.0 hrs/day) × # of Replenishment Intervals/hr (4 int/hr)) × (1-((1-Saliva Extraction Factor (0.5))^(Number of Hand-to-Mouth Events per Hour (20 events/hr)) ÷ (# of Replenishment Intervals/hr))] / [Body Weight (11 kg child 1 to < 2 years old years old)]
   Where the Hand Residue Loading (mg/cm^2) = [$F_{ai_{hands}}$ (Solid, 0.37; Liquids; 0.040) x Dermal Exposure (mg/day)] ÷ [Surface Area of 1 Child Hand (150 cm^2) x 2]

Table E.2. Residential Post-Application Non-Cancer Risk Estimates from Use of TCVP Pet Collars Assuming 99.62% Liquid/0.38% Dust Ratio Formulation.

EPA Reg. No./ Animal	Lifestage	Application Rate (mg ai)[1]	Animal Size	Liquid Incidental Oral Dose (mg/kg/day)[2]	Dust Incidental Oral Dose (mg/kg/day)[3]	Combined Dose[4] (99.62%/0.38% Liquid/Dust) (mg/kg/day)	99.62% Liquid/0.38% Dust Combined Incidental Oral MOE **(LOC = 1000)**[5]
2596-49: Cat	Children 1 < 2	1,320	Small	0.0019	0.48	0.0037	**750**
			Medium	0.0011	0.29	0.0022	1300
			Large	0.0007	0.18	0.0014	2000
2596-50, 62: Dog	Children 1 < 2	2,219	Small	0.0016	0.40	0.0031	**900**
		3,738	Large	0.0007	0.18	0.0014	2000
2596-63: Cat	Children 1 < 2	1,752	Small	0.0025	0.63	0.0049	**570**
		1,986	Large	0.0011	0.27	0.0021	1300
2596-83: Cat	Children 1 < 2	1,402	Small	0.0020	0.51	0.0039	**710**
		2,161	Medium	0.0019	0.47	0.0036	**770**
		2,920	Large	0.0016	0.40	0.0031	**910**
2596-84: Dog	Children 1 < 2	2,219	Small	0.0016	0.40	0.0031	**900**
		3,738	Large	0.0007	0.18	0.0014	2000
2596-139: Cat	Children 1 < 2	1,168	Small	0.0017	0.42	0.0033	**850**
			Medium	0.0010	0.25	0.0020	1,400
			Large	0.0006	0.16	0.0012	2,300
2596-139: Dog	Children 1 < 2	5,840	Small	0.0042	1.06	0.0082	**340**
			Medium	0.0018	0.45	0.0035	**790**
			Large	0.0011	0.29	0.0022	1,200

1. Application rates are label defined. Refer to Table A.2.
2. Liquid HTM Doses from Table E.1.
3. Dust HTM Doses from Table E.1.
4. 99.62% Liquid/0.38% Dust Combined Dose (mg/kg/day) = (Liquid HtM Dose * 0.9962) + (Dust HtM Dose * 0.0038).
5. 99.62% Liquid/0.38% Dust Combined MOE = Incidental Oral NOAEL (2.8 mg/kg/day) ÷ Combined Dose (mg/kg/day).

Table E.3. Residential Post-Application Non-Cancer Risk Estimates from Use of TCVP Dust/Powder and Liquid Spray Formulations.

EPA Reg. No./ Animal	Lifestage	Application Rate (mg ai)[1]	Animal Size	Dermal Exposure (mg/day)[2]	Incidental Oral Dose (mg/kg/day)[3]	Incidental Oral MOE **(LOC = 1000)**[4]
Dusts/Powders						
47000-123: Dog	Children 1 < 2	170	Small	1.0	0.0087	**320**
		430	Medium	1.1	0.0093	**300**
		680	Large	1.1	0.0095	**300**
47000-123: Cat	Children 1 < 2	43	Small	0.52	0.0043	**640**
		100	Medium	0.74	0.0063	**450**
		150	Large	0.70	0.0059	**480**
2596-78: Cat	Children 1 < 2	280	Small	3.4	0.0287	**98**
		470	Large	2.1	0.0180	**160**
2596-79: Dog	Children 1 < 2	470	Small	2.9	0.0240	**120**
		940	Medium	2.4	0.0205	**140**
		1,200	Large	1.9	0.0163	**170**

Table E.3. Residential Post-Application Non-Cancer Risk Estimates from Use of TCVP Dust/Powder and Liquid Spray Formulations.						
EPA Reg. No./ Animal	Lifestage	Application Rate (mg ai)[1]	Animal Size	Dermal Exposure (mg/day)[2]	Incidental Oral Dose (mg/kg/day)[3]	Incidental Oral MOE **(LOC = 1000)**[4]
Liquid (Pump/Trigger) Sprays						
2596-126, 140: Cat (Trigger)	Children 1 < 2	250	Small	1.9	0.00172	1,600
		350	Large	0.99	0.00090	3,100
2596-140: Cat (Pump)	Children 1 < 2	51	Small	0.39	0.00035	8,000
		71	Large	0.20	0.00018	15,000
2596-125, -140: Dog (Trigger)	Children 1 < 2	350	Small	1.3	0.00120	2,300
		400	Medium	0.65	0.00059	4,800
		700	Large	0.72	0.00066	4,300

1. Application rates are label defined. Refer to Table A.2.
2. Dermal Exposure (mg/day) = [Transfer Coefficient (cm^2/hr)] * [Application Rate (label defined) * Fraction Application Rate (Dust, 0.00048; Spray, 0.0081) ÷ Surface Area of Cat/Dog (Cat: Small, 1,500; Medium, 2,500; Large, 4,000 cm^2 - Dog: Small, 3,000; Medium, 7,000; Large, 11,000 cm^2)] x [Exposure Time (Adults, 0.77 hours/day; Children, 1.0 hours/day))]
3. Incidental Oral Dose (mg/kg/day) = [Hand Residue Loading (mg/cm^2)] × [Fraction of Hand Mouthed (0.13) × Surface Area of 1 Child Hand (150 cm^2)] x [Exposure Time (1.0 hrs/day) × # of Replenishment Intervals/hr (4 int/hr)) × (1-((1-Saliva Extraction Factor (0.5))^(Number of Hand-to-Mouth Events per Hour (20 events/hr)) ÷ (# of Replenishment Intervals/hr))] / [Body Weight (11 kg child 1 to < 2 years old years old)]
   Where the Hand Residue Loading (mg/cm^2) = [Fai_{hands} (Dusts, 0.37; Liquids; 0.040) x Dermal Exposure (mg/day)] ÷ [Surface Area of 1 Child Hand (150 cm^2) x 2]
4. MOE = Incidental Oral NOAEL (2.8 mg/kg/day) ÷ Incidental Oral Dose (mg/kg/day).

Appendix F – Summary of Residential Post-Application Cancer Exposure and Risks

Table F.1. Residential Post-Application Cancer Risk Estimates from Use of TCVP Pet Collars Assuming 99.62% Liquid/0.38% Dust Ratio Formulation.

Table F.2. Residential Post-Application Cancer Estimates from Use of TCVP Dust/Powder and Liquid Spray Formulations.

Table F.1. Residential Post-Application Cancer Risk Estimates from Use of TCVP Pet Collars Assuming 99.62% Liquid/0.38% Dust Ratio Formulation.

Animal Type	Animal Size	Lifestage	Liquid LADD[1]	Dust LADD[2]	Combined 99.62% Liquid/0.38% Dust LADD[3]	Cancer Risk Estimate[4]
2596-49: Cat	Small	Adult	1.4E-03	3.8E-02	1.6E-03	2.9E-06
	Medium		8.5E-04	2.3E-02	9.4E-04	1.7E-06
	Large		5.3E-04	1.4E-02	5.9E-04	1.1E-06
2596-50.62: Dog	Small		1.2E-03	3.2E-02	1.3E-03	2.4E-06
	Large		5.5E-04	1.5E-02	6.0E-04	1.1E-06
2596-63: Cat	Small		1.9E-03	5.1E-02	2.1E-03	3.8E-06
	Large		8.0E-04	2.2E-02	8.8E-04	1.6E-06
2596-83: Cat	Small		1.5E-03	4.1E-02	1.7E-03	3.0E-06
	Medium		1.4E-03	3.8E-02	1.5E-03	2.8E-06
	Large		1.2E-03	3.2E-02	1.3E-03	2.4E-06
2596-84: Dog	Small		1.2E-03	3.2E-02	1.3E-03	2.4E-06
	Large		5.5E-04	1.5E-02	6.0E-04	1.1E-06
2596-139: Cat	Small		1.3E-03	3.4E-02	1.4E-03	2.5E-06
	Medium		7.5E-04	2.0E-02	8.3E-04	1.5E-06
	Large		4.7E-04	1.3E-02	5.2E-04	9.5E-07
2596-139: Dog	Small		3.1E-03	8.5E-02	3.5E-03	6.3E-06
	Medium		1.3E-03	3.6E-02	1.5E-03	2.7E-06
	Large		8.6E-04	2.3E-02	9.4E-04	1.7E-06

1 Liquid LADD = [Dermal Dose (mg/kg/day)] × [Days per year of exposure (180 days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (50 yrs) ÷ Lifetime expectancy (78 yrs)]. Dermal dose calculated using fraction transferred value from Davis study of 0.00092.

2 Dust LADD = [Dermal Dose (mg/kg/day)] × [Days per year of exposure (180 days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (50 yrs) ÷ Lifetime expectancy (78 yrs)]

3 Combined 99.62% Liquid/0.38% Dust LADD = (Liquid LADD * 0.9962) + (Dust LADD * 0.0038).

4 Cancer risk estimates = Combined 99.62% Liquid/0 38% Dust LADD × Q_1^*, where $Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$

Table F.2. Residential Post-Application Cancer Estimates from Use of TCVP Dust/Powder and Liquid Spray Formulations.

Animal Type	Animal Size	Lifestage	Total LADD[1,2]	Cancer Risk Estimate[3]
Dust/Powder				
47000-123: Dog	Small	Adult	5.9E-04	1.1E-06
	Medium		6.3E-04	1.2E-06
	Large		6.4E-04	1.2E-06
47000-123: Cat	Small		2.9E-04	5.4E-07
	Medium		4.2E-04	7.8E-07
	Large		4.0E-04	7.3E-07
2596-78: Cat	Small		1.9E-03	3.6E-06
	Large		1.2E-03	2.2E-06
2596-79: Dog	Small		1.6E-03	3.0E-06
	Medium		1.4E-03	2.5E-06
	Large		1.1E-03	2.0E-06
Liquid (Pump/Trigger) Spray				
2596-126, 140: Cat (Trigger)	Small	Adult	5.3E-04	9.6E-07
	Large		2.8E-04	5.1E-07
2596-140: Cat (Pump)	Small		1.1E-04	2.0E-07
	Large		5.6E-05	1.0E-07
2596-125, -140: Dog (Trigger)	Small		3.7E-04	6.7E-07
	Medium		1.8E-04	3.3E-07
	Large		2.0E-04	3.7E-07

1 Total Lifetime Average Daily Dose (mg/kg/day) = Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day).

2 Dermal and Inhalation LADD equations provided in Appendix B.

3 Cancer risk estimates = Total LADD × Q1*, where Q1* = 1.83×10^{-3} $(mg/kg/day)^{-1}$

Appendix G. Summary of Residue Data Used in TCVP Pet Collar Assessments

In the 2014 residential risk assessment for TCVP, a propoxur pet collar residue transfer study (MRID 48589901) was used for assessment of post-application risks from TCVP pet collars. Subsequent to the completion of the 2014 residential risk assessment, an amitraz pet collar residue transfer study was submitted to EPA (MRID 49468801). Based on the review of the amitraz pet collar study, it was determined that the mean Day 0 residue transfer resulting from the amitraz pet collar exceeded the mean residue transfer measured on Day 0 from the propoxur pet collar. As a result, HED updated the risk estimates for exposures resulting from contact with a TCVP pet collar-treated pet using the amitraz pet collar transfer study.

The Davis study publication was considered for use in the assessments due to arguments submitted by NRDC in its August 5th, 2015, Opening Brief in *NRDC v. EPA*, Case No. 15-70025 (9th Cir.) (Opening Brief). NRDC's Opening Brief was filed in litigation challenging EPA's November 6, 2014 denial of NRDC's 2009 Petition to cancel all TCVP pet products[27]; the denial was based on the 2014 residential pet product assessment. The Agency provided a point-by-point response to the NRDC's arguments in a December 21, 2015 memorandum,[28] issued in conjunction with the 2015 draft TCVP risk assessment for Registration Review. Among the arguments presented by the NRDC was that the Agency "failed to consider the Davis study for the estimation of post-application risks for exposures to the TCVP pet collar." In its 2015 memorandum, the Agency acknowledged consideration of the potential effect of using the Davis study as the basis for residential post-application assessment of exposures from TCVP pet collars, the study was reviewed,[29] an OPP ethics review was conducted[30], and preliminary risk estimates were presented with use of these data. However, the formal use of the Davis study was put on hold pending review by EPA's HSRB in January 2016. The Davis study includes 1) glove residue data collected by adult volunteers petting TCVP treated dogs 2) plasma cholinesterase (ChE) measures from treated dogs 3) tee shirt samples collected from children exposed to TCVP treated dogs and 4) urinary biomonitoring for adults and children exposure to TCVP treated dogs. However, for purposes of the TCVP risk assessment, EPA may rely only on the transferable residue data [in light of 40 CFR Part 26, subpart Q regarding ethical standards for assessing whether to rely on the results in human research in EPA actions] as these are the only data from the study that result in the potential for greater risks, are applicable to human exposures (in the case of the dog plasma ChE measures), or in the case of the urinary biomonitoring data, are useful given current scientific limitations (i.e., a physiologically based pharmacokinetic (PBPK) model applicable to TCVP). While EPA proposed to rely only on the glove residue data (which did not involve children), since these data were collected as part of broader research which did involve children, HSRB review was necessary.

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[27] Natural Resources Defense Council, Inc., Petitioner, v. U.S. Environmental Protection Agency, Respondent. On Petition to Review of an Order of the U.S. Environmental Protection Agency. In the United State Court of Appeals for the Ninth Circuit. 8/5/2015. No. 15-70025.

[28] W. Britton. Tetrachlorvinphos (TCVP): Responses to Arguments Presented in the Natural Resources Defense Council, Inc.'s (NRDC) Aug. 5, 2015 Opening Brief in *NRDC v. EPA*, Case No. 15-70025 (9th Cir.). 12/21/2015, D430589.

[29] W. Britton. Science Review of "Davis et al., 2008. Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos" for HSRB Consideration. D430707. 12/16/2015.

[30] M. Lydon. Ethics Review of Davis et al Research on Flea Collars with TCVP. 12/15/2015.

On January 12-13, 2016, the EPA HSRB addressed the scientific and ethical charge questions related to Davis study. Ethics and science reviews were conducted by the Agency in support of the HSRB meeting. [31,32] A Federal Register (FR) notice was published on April 11, 2016, providing the following information: EPA's proposal to rely on the Davis study; the reason for review by HSRB; the background on ethical conduct of research; summary of discussion on ethics-related questions; the standards applicable to ethical conduct and reliance on data; and the availability of HSRB meeting materials.[33]

The HSRB concluded that, "The research is scientifically sound and, if used appropriately, the pet fur transferable residue data from the rubbing protocol used in the study can provide useful information for evaluating potential exposures of adults and children from contact with dogs treated with tetrachlorvinphos containing pet collars."[34] Per EPA's response to NRDC's Opening Brief arguments, "EPA would rely on these data (Davis study) for regulatory decision making if HSRB determines that the study is scientifically valid and it meets appropriate human ethics requirements," since these data result in in greater potential risks than those estimated using the amitraz pet collar residue transfer study (which had been relied upon in the previous risk assessments) and are, therefore, more protective of human health. Accordingly, post-application risks were assessed with use of the Davis study data only in the 2016 ORE assessment.

The use of the Davis study as the primary data source was consistent with, and supported by, the recommendations from the comments following the 2015 draft ORE assessment for Registration Review including those submitted by NRDC and the Hartz Mountain Corporation. Per NRDC, "the Davis Study has met the appropriate scientific and ethical criteria and should be relied upon for the evaluation of exposures from TCVP containing flea collars" and the Hartz Mountain Corporation describes that, "the glove residue data measured in the Davis et al. (2008) study are valuable because they represent actual measurements of TCVP transfer from dogs wearing commercial collars to the hands of individuals petting them." Further, the NRDC states that, "EPA's utilization of transferable residue data from the amitraz study is not supported by the evidence and should not be relied upon to evaluate risk."

In 2019, Hartz Mountain submitted a TCVP-specific residue transfer study that has also been reviewed by HED and determine to be acceptable for risk assessment (MRID 50881801[35]). Both studies are representative of potential exposure to currently registered TCVP pet collars; however, the Davis study indicates a greater fraction transfer value than MRID 50881801, but the latter study only had a limited number of samples (i.e., a total of 9 dogs with only 3 dogs per petting simulation group). Due to the fact that (1) both available studies are representative of current TCVP pet collars and have been considered acceptable for risk assessment, (2) the Davis

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[31] M. Lydon. Ethics Review of Davis et al Research on Flea Collars with TCVP. 12/15/2015.
[32] W. Britton. Science Review of "Davis et al., 2008. Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos" for HSRB Consideration. D430707. 12/16/2015.
[33] https://www.federalregister.gov/documents/2016/04/11/2016-08281/tetrachlorvinphos-tcvp-epa-proposal-to-rely-on-data-from-human-research-on-tcvp-exposure-from-flea
[34] Letter from Liza Dawson, PhD, Chair of the EPA HSRB to Thomas Burke, PhD, MPH, EPA Science Advisor. Subject: January 12-13, 2016 EPA Human Studies Review Board Meeting Report. March 30, 2016.
[35] MRID 50881801. D453149, K. Lowe et al., 12/05/2019.

study provides a more protective assessment of potential exposure, and (3) in consideration of the limited sample size in MRID 50881801, HED has presented risk estimates utilizing both data sets.

A summary of the Davis study and MRID 50881801 is provided below.

Davis Study - *Davis, M., et al. Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos. Journal of Exposure Science and Environmental Epidemiology. (2008) 18, 564-570).*

The journal article, Davis et al., 2008, was conducted with the purpose of investigating the exposures to TCVP that could occur in children and adults from the use of a TCVP-containing collar on pet dogs. A single product was tested, Hartz Mountain Ultimate Flea Collar, which is composed of 14.55% TCVP. Two separate studies were conducted with the test product as a part of the journal article. Both were conducted in Oktibbeha County, Mississippi, with volunteer households having pet dogs.

Study 1: The first study was conducted for approximately 4 months (112 days) and evaluated the time course of TCVP residue transfer (peak residue and dissipation) to white cotton gloves used to rub, or pet, the dogs' fur. Twenty-three dogs of different breeds and weights were treated with the TCVP flea collar in study 1. Dogs were petted by volunteers continuously for a 5-minute period with use of a cotton glove in following with a defined rubbing protocol. Although not described in the article, it was deduced that the rubbing protocol was repeated for each dog/volunteer to result in a measure of transferable residue 1) from the fur of the neck (rubbing over the collar), 2) from the fur of the neck (with the collar removed), and 3) along the back of the dog in the tail region. Study 1 also analyzed plasma cholinesterase (ChE) activity from blood samples taken from each dog at the same time as the rubbing samples. Pre-collar and post-collar application samples were collected for the evaluation of residue transfer to gloves and the dogs' blood ChE activity.

Significant increases in transferable TCVP residues were observed on the cotton gloves used to pet dogs compared to pretreatment concentrations. In study 1, transferable residues from all three sampling locations decreased (86% decline) throughout the 112 days following a peak at day 7 post-collar application, 24,000 ± 4,000 µg/glove over the collar. Similar trends were also observed in detectable residues around the neck without the collar in place and in the tail region where there were 94% and 71% decreases, respectively. Mean glove residues for all sampling times were 14,300 µg/glove over the collar, 4,300 µg/glove on the neck with the collar removed, and 130 µg/glove in the tail region. No significant changes in dog plasma ChE were measured.

Study 2: The second, subsequent study was conducted on the basis that results from study 1 indicated that TCVP residues peaked and then suddenly dropped within 3 weeks of collar placement. Therefore, the second study was conducted over a 3 week (21 day) period, and included human biomonitoring of the TCVP metabolite, 2,4,5-trichloromandelic acid (TCMA), in urine of adults and children. The second study also measured TCVP residues as transferred from treated dogs to cotton t-shirts worn by children, as well as those transferred to cotton gloves

from petting the dogs' fur. Pre- and post-collar samples were collected for the residue collection by glove, t-shirt, and the biomonitoring phase of study 2.

In study 2, TCVP residues obtained over the collar and around the neck without the collar in place decreased (30% decline) from 5 to 12 days post-collar application, while residues obtained from the tail region remained fairly constant (81 µg/glove at 5 days and 82 µg/glove at 12 days). The peak transferable residues collected over the collar at 5 days post-collar application were of a similar magnitude to those observed in study 1. Mean residues (for all gloves analyzed) post-collar application were 19,000 µg/glove over the collar, 8,000 µg/glove on the neck with the collar removed, and 80 µg/glove in the tail region.

The average amount of TCVP residues detected on children's t-shirts on sampling days 7-11 post-collar application was 1.8 ± 0.8 µg/shirt, with no significant differences among the sampling days. Transferable residues were significantly greater than the mean pre-treatment residue of 0.03 ± 0.006 µg/shirt.

Urine samples collected from children generally contained more urinary TCMA than that from the adults with significant differences between the ages occurring on only 1 of the 5 sampling days (day 11). The ranges of TCMA concentrations were large across all adults and children; 1.4 - 582 ng/ml urine for adults, and 2.1 - 1,558 ng/ml urine in children. However, no significant differences in urinary TCMA concentrations were observed within each adult or child in the study. The urinary TCMA concentrations were all adjusted for creatinine content; however, there were no differences in outcomes and, as a result, reported values were unadjusted. No significant correlations were identified among t-shirt TCVP residues, the amount of time spent with treated dogs, and urinary TCMA concentrations.

MRID 50931601. D454190, K. Lowe et al., 12/03/2019. Submitted in response to GDCI-083702-1791.

In 2019, Hartz Mountain Corporation submitted a TCVP-specific residue transfer study for pet collars (MRID 50881801). The purpose of the study was to measure the transferability of the test substance (TCVP) and a plasticizing agent from the hair of a dog wearing a TCVP-impregnated collar. Each collar contained 14.55% TCVP (TCVP wt/collar wt). The collars are typically applied to dogs by securing the collar around the dog's neck and cutting off any excess collar length.

A total of 9 dogs were used in the study, randomly assigned to 3 groups. Each group had different assigned number of simulations. Dogs in Group 1 were petted for 5 simulations, dogs in Group 2 received 10 petting simulations, and dogs in Group 3 received 25 petting simulations. Each simulation consisted of three strokes conducted using a mannequin hand fitted with three cotton gloves. The first stroke was on the right side, the second on the left side, and the third was along the back line. After the simulations, all 3 gloves were removed and placed individually into labeled jars. Samples were collected from each dog 4 days prior to application of the collar (4 days prior to treatment or -4DAT) and 10 days after application of the collar (10DAT). In addition, at the end of the study, each collar used on the animals was collected, stored in separate containers, and sent to the analytical testing laboratory facility.

Fortification samples were prepared on -4DAT and 10DAT. Duplicate samples were fortified with each analyte at three levels: 120 µg/sample (LOQ), 2,000 µg/sample, and 4,400 µg/sample. Fortified samples were handled, stored and shipped in the same manner as the residue samples. Average recoveries for the low-, mid- and high-level fortified samples ranged from 87.3 – 114% for TCVP on sampling day 10 and from 82.5-105% for the inert.

Glove samples collected prior to the application (-4DAT) did not have any detectable residues and are not discussed herein. HED corrected the 10-DAT field samples using the 10-DAT field fortification recoveries. Residues ≤660 µg were corrected for the average low level field fortification recovery (87.3% for TCVP and 82.5% for the inert); residues >2,800 µg were corrected for the average high level field fortification recovery (106% for TCVP and 100% for the inert); and residues between 600 µg and 2,800 µg were corrected for the average mid-level field fortification recovery (114% for TCVP and 105% for the inert). HED calculated residues in µg/glove, µg/cm^2 of dog surface area, percent of initial TCVP in collar, and percent of applied dose transferred.

The difference between the initial collar weight and the end weight was multiplied by the percent active ingredient in the collar (14.55%) to calculate the actual dose applied. The actual dose applied ranged from 0.052 to 0.2639 g ai (51,914 to 268,622 µg ai). In addition, HED calculated the initial TCVP in the collar by multiplying the percent active ingredient in the collar (14.55%) by the initial weight of the collar. The initial TCVP in the collar ranged from 2.52 to 3.05 g ai (2,524,192 to 3,048,429 µg ai).

The highest average residues of TCVP occurred on gloves after 20 petting simulations (Group 3) at 4,527.5 µg/gloves (5.98% of applied dose and 0.886 µg/cm^2). The lowest average residues of TCVP were observed on gloves from Group 2 (10 petting simulations) at 2,512.9 µg/gloves (1.53% of applied dose and 0.456 µg/cm^2). For the inert, average residues were highest on gloves from Group 3 (20 petting simulations) at 473.9 µg/gloves. The relative ratio of TCVP/the inert ranged from 7.0 to 14.5; the highest average ratio was observed in Group 2 at 12.9.

Percent transferable residues of TCVP based on the initial TCVP in the collar ranged from 0.049% to 0.228%; average percent transferable residues of TCVP were 0.098% for Group 1 (5 petting simulations), 0.086% for Group 2 (10 petting simulations), and 0.167% for Group 3 (25 petting simulations).

Percent transferable residues of applied TCVP dose ranged from 0.93% to 6.83%; average percent transferable residues of applied TCVP were 2.38% for Group 1 (5 petting simulations), 1.53% for Group 2 (10 petting simulations), and 5.98% for Group 3 (25 petting simulations).

Attachment C. Tetrachlorvinphos: Addendum to the Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: July 20, 2020

SUBJECT: Tetrachlorvinphos: Addendum to the Revised Residential Exposure and Risk Assessment for the Registered Pet Product Uses.

PC Code: 083701, 083702
Decision No.: 559447
Petition No.: N/A
Risk Assessment Type: Residential Exposure Assessment
TXR No.: NA
MRID No.: NA

DP Barcode: D458466
Registration Nos.: NA
Regulatory Action: Registration Review
Case No.: 1321

CAS No.: 961-11-5, 22248-79-9
40 CFR: NA

FROM: Kelly Lowe, Environmental Scientist
Risk Assessment Branch V/VII (RAB V/VII)
Health Effects Division (HED; 7509P)
Office of Pesticide Programs

THROUGH: Michael Metzger, Chief
RABV and RABVII/HED (7509P)

And

Wade Britton, MPH, Environmental Health Scientist
Risk Assessment Branch IV (RABIV)

TO: Patricia Biggio, Chemical Review Manager
Dana Friedman, Branch Chief
Risk Management and Implementation Branch I (RMIBI)
Pesticide Re-evaluation Division (PRD; 7508P)
Office of Pesticide Programs

Introduction

The attached document is an addendum to the residential risk assessment for the pet uses of tetrachlorvinphos (TCVP) (D457031, K. Lowe, 7/20/2020). As a result of the risks of concern identified in that risk assessment, the registrant proposed several mitigation measures. This

memorandum summarizes the mitigation measures and presents revised risk estimates for the registered pet collar uses.

Updated TCVP Pet Use Risk Estimates

In the 2020 TCVP pet use risk assessment (D457031, K. Lowe, 7/20/2020), risk estimates of concern were identified for all dust/powder products and for some pet collars for some pet sizes. As a result, the registrant has proposed several mitigation measures to address those concerns. These include:

- Cancellation of all dust/powder products
- Cancellation of pet collar product, EPA Reg. # 2596-63
- Amendment of pet collar products EPA Reg.# 2596-49, 2596-83 and 2596-139 to restrict use to cats and kittens weighing above 5 pounds
- Redesign of pet collar products EPA Reg. # 2596-50, 2596-62, 2596-83, 2596-84 and 2596-139 to reduce weight of the collars (i.e., to reduce the amount of active ingredient applied)

A revised use profile table with updated application rates for the pet collars is provided below (Table 2). Taking into account the pet collar mitigation measures, HED has recalculated the residential handler and post-application risk estimates and the revised MOEs are not of concern (i.e., all MOEs ≥ the LOCs of 300 for inhalation and 1000 for incidental oral). These are presented in Table 1 below.

Table 1. Summary of TCVP Pet Product Residential Risk Estimates (post-mitigation)

Reg. No. (Target Animal)	Size of Animal	Residential Handler Non-cancer MOEs (LOC = 300)	Residential Handler Cancer Risk Estimates	Residential Post-application MOEs (LOC = 1000)	Residential Post-application Cancer Risk Estimates
Pet Collars					
2596-49 (Cat)	Medium	1,100,000	1.6E-08	1,300	1.7E-06
	Large			2,000	1.1E-06
2596-50, 62 (Dog)	Small	900,000	1.9E-08	1,300	1.7E-06
	Large	500,000	3.4E-08	2,600	8.2E-07
2596-83 (Cat)	Medium	1,200,000	1.4E-08	1,500	1.6E-06
	Large	900,000	1.9E-08	1,700	1.3E-06
2596-84 (Dog)	Small	900,000	1.9E-08	1,300	1.7E-06
	Large	500,000	3.4E-08	2,600	8.2E-07
2596-139 (Cat)	Medium	1,200,000	1.4E-08	1,500	1.6E-06
	Large	900,000	1.9E-08	1,700	1.3E-06
2596-139 (Dog)	Small	900,000	1.9E-08	1,300	1.7E-06
	Medium	650,000	2.7E-08	2,200	1.0E-06
	Large	500,000	3.4E-08	2,600	8.2E-07
Application of TCVP Liquid Sprays					
2596-126, -140 (Cat) (Trigger)	Small	25,000	2.5E-08	1,600	9.6E-07
	Large	18,000	3.5E-08	3,100	5.1E-07
2596-140 (Cat) (Pump)	Small	120,000	5.1E-09	8,000	2.0E-07
	Large	87,000	7.2E-09	15,000	1.0E-07
2596-125, -140 (Dog) (Trigger)	Small	18,000	3.5E-08	2,300	6.7E-07
	Medium	16,000	4.0E-08	4,800	3.3E-07
	Large	8,900	7.0E-08	4,300	3.7E-07

Table 2. Summary of TCVP Occupational/Residential Pet Products			
EPA Reg. No.	Use Site	Application Rate	Use Restrictions
Collars			
2596-49 (collar weight: 0.40 oz)	Cats	11.3 gram collar = 0.40 oz (14.6 % ai) Total ai: 0.0036 lb ai or 1,650 mg ai 20% removed: 1,320 mg ai	Do not use in kittens under 12 weeks of age and cats/kitten weighing less than 5 lbs. Place the collar around the cat's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 3 months, every 2 months for severe infestation.
2596-50 (collar weight: 0.46 – 0.84 oz)	Dogs	13.2 gram collar = 0.46 oz (14.6 % ai) Total ai: 0.0042 lb ai or 1,927 mg ai 20% removed: 1,542 mg ai	Do not use on puppies less than 6 weeks of age. Place the collar around the dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 3 months, every 2 months for severe infestation.
2596-62 (collar weight: 0.46 – 0.84 oz)		23.7 gram collar = 0.84 oz (14.6 % ai) Total ai: 0.0076 lb ai or 3,460 mg ai 20% removed: 2,768 mg ai	
2596-83 (collar weight: 0.34 - 0.47 oz)	Cats	9.68 gram collar = 0.34 oz (14.6% ai) Total ai: 0.0031 lb ai or 1,413 mg ai 20% removed: 1,131 13.2 gram collar = 0.47 oz (14.6% ai) Total ai: 0.0042 lb ai or 1,927 mg ai 20% removed: 1,542 mg ai	Do not use in kittens under 12 weeks of age and cats/kitten weighing less than 5 lbs. Place the collar around the cat's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 7 months, every 5 months for severe infestation.
2596-84 (collar weight: 0.46 – 0.84 oz)	Dogs	13.2 gram collar = 0.46 oz (14.6% ai) Total ai: 0.0042 lb ai or 1,927 mg ai 20% removed: 1,542 mg ai 23.7 gram collar = 0.84 oz (14.6% ai) Total ai: 0.0076 lb ai or 3,460 mg ai 20% removed: 2,768 mg ai	Do not use on puppies under 6 weeks of age. Place the collar around the dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 7 months, every 5 months for severe infestation.
2596-139 (collar weight: 0.34 – 0.46 oz[1])	Cats	9.68 gram collar = 0.34 oz (14.6% ai) Total ai: 0.0031 lb ai or 1,413 mg ai 20% removed: 1,131 mg ai 13.2 gram collar = 0.46 oz (14.6% ai) Total ai: 0.0042 lb ai or 1,927 mg ai 20% removed: 1,542 mg ai	Do not use on puppies under 6 weeks old/ kittens under 12 weeks old, and weighing less than 5 lbs. Place the collar around the cat's/dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 7 months, or more frequently for severe infestation.
2596-139 (collar weight: 0.46 – 0.84 oz[1])	Dogs	13.2 gram collar = 0.46 oz (14.6% ai) Total ai: 0.0042 lb ai or 1,927 mg ai 20% removed: 1,542 mg ai 23.7 gram collar = 0.84 oz (14.6% ai) Total ai: 0.0076 lb ai or 3,460 mg ai 20% removed: 2,768 mg ai	Do not use on puppies under 6 weeks old/ kittens under 12 weeks old. Place the collar around the cat's/dog's neck, adjust for proper fit, and buckle in place. Leave 2 or 3 inches on the collar for extra adjustment and cut off and dispose of the extra length. Replace the collar every 7 months, or more frequently for severe infestation.

Table 2. Summary of TCVP Occupational/Residential Pet Products			
EPA Reg. No.	Use Site	Application Rate	Use Restrictions
Pump/Trigger Sprays[2]			
2596-125	Dogs (Trigger)	1.1% ai Small: 30 strokes = 27.78 grams product = 0.00066 lb ai or 300 mg ai Medium: 40 strokes = 37.04 grams product = 0.00088 lb ai or 400 mg ai Large: 70 strokes = 64.82 grams product = 0.0015 lb ai or 700 mg ai, large	Do not apply to pets (puppies) less than 6 weeks old. Hold bottle upright about 6 inches from pet. Spray lightly until the tips of the pet's hair are moist. Rub spray into animal's coat. Repeat once per week. Recommended dosage: Spray 25-30 strokes for a small dog. Spray 30-40 strokes for a medium dog. Spray 40-70 strokes for a large dog. More spray may be needed for longhaired dogs. [3]
2596-126	Cats (Trigger)	1.1% ai Small: 25 strokes = 23.15 grams product = 0.00055 lb ai or 250 mg ai Large: 35 strokes = 32.41 grams product = 0.00077 lb ai or 350 mg ai	Do not apply to pets (kittens) less than 6 weeks old. Hold bottle upright about 6 inches from pet. Spray lightly until the tips of the pet's hair are moist. Rub spray into animal's coat. Repeat once per week. Recommended dosage: Spray 15-25 strokes for a small cat. Spray 25-35 strokes for a large cat. More spray may be needed for longhaired cats. [3]
2596-140	Cats[5] (Pump)	1.1% ai Small: 25 strokes = 4.73 grams product = 0.00011 lb ai or 51 mg ai Large: 35 strokes = 6.62 grams product = 0.00016 lb ai or 71 mg ai	Do not use on puppies or kittens less than 12 weeks old. Hold bottle upright about 6 inches from pet. Spray lightly until the tips of the pet's hair are moist. Rub spray into animal's coat. Repeat once per week. Recommended dosage: Spray 15-25 strokes for a small cat. Spray 25-35 strokes for a large cat.[4] Recommended dosage: Spray 25-35 strokes for a small dog. Spray 30-40 strokes for a medium dog. Spray 40-70 strokes for a large dog.[4]
	Cats[5] (Trigger)	1.1% ai Small: 25 strokes = 23.15 grams product = 0.00055 lb ai or 250 mg ai Large: 35 strokes = 32.41 grams product = 0.00077 lb ai or 350 mg ai	
	Dogs (Trigger)	1.1% ai Small: 35 strokes = 32.41 grams product = 0.00077 lb ai or 350 mg ai Medium: 40 strokes = 37.04 grams product = 0.00088 lb ai or 400 mg ai Large: 70 strokes = 64.82 grams product = 0.0015 lb ai or 700 mg ai	

1. Based on updated labels: (1) cat collar length ranges from 11 to 15 inches and collar weighs 0.88 g/inch = 9.68 – 13.2 g (0.34 – 0.46 oz) and (2) dog collar length ranges from 15 to 27 inches and collar weighs 0.88 g/inch = 13.2 – 23.76 g (0.46 – 0.84 oz)
2. Application rates for liquid spray products determined using information provided by the Registrant regarding the volume of product released per stroke: pump spray products = 0.19 g and trigger-spray products = 0.93 g.
3. Current label language (EPA Reg. No. 2596-125 and 2596-126) allows for more than a prescribed amount of strokes per cat/dog. Assessment is based on the amount labelled for each weight range. Any such label language allowing for an exceedance should be removed.
4. The recommended number of strokes as presented for EPA Reg. No. 2596-140 is based on master label amendments proposed by the registrant and granted by EPA (March 2014). Previously, a number of strokes per cat/dog was not recommended. The maximum number of strokes was considered in the risk assessment for cats and dogs based on animal size.
5. EPA Reg. No. 2596-140 registered as both a pump spray and trigger spray for cats.